NUTRITIONAL ARMOUR IN EVOLUTION: DOCOSAHEXAENOIC AS A DETERMINANT OF NEURAL EVOLUTION AND HOMINID BRAIN DEVELOPMENT

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ABSTRACT

There is a common view that lipids in the cell membrane are barriers separating two aqueous phases. By contrast, it is most likely that lipids were key players in the earliest evolution of the animals and still today act as determinants of human development. The lipids of photoreceptors of the cephalopods, fish, amphibia, reptile, birds and mammals are consistently dominated (>50% of acyl groups) by the same high levels of docosahexaenoic acid (DHA). The genomes of these species reflects at least a 500 million year span of evolution providing the most compelling evidence for the essentiality of DHA for the photoreceptor. Similarly, we find a close identity with DHA dominating the inner cell membrane composition of the brain in 42 mammalian species. This consistency is despite the metabolic precursor for DHA having the same structure except for missing two adjacent protons. This striking conservation is an example of Darwin's "Conditions of Existence" which he described as the higher force in evolution. The human genome separated from the chimpanzee 5-7 mya. Hence humans are adapted to wild foods. Sight of this reality has been lost in the modern food system which prioritises protein and body growth and has distanced the dietary fats form the balanced diet that drove cerebral expansion. The balanced diet of 1 or 2 to 1 ω6 to ω3 essential fatty acids has been altered to a great excess of ω6 linloeic acid, saturated and trans isomer fats. A sign that this alteration does not meet the priority for sustainability of human mental health is seen in the rise in brain disorders which have now overtaken all other burdens of ill health in the West. Addressing this clear and present threat to humanity is the greatest challenge of today.

Key words: evolution, genomics, lipids, docosahexaenoic, arachidonic, ω 6, ω 3, brain, vascular development, cerebral expansion, Darwin, fish, sea food, marine ingredients, oceanic agriculture, sustainability of humanity

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Introduction

Docosahexaenoic acid (all-cis-docosa-4,7,10,13,16,19-hexaenoic acid – C22:6ω3, DHA) is a major, essential fatty acid, functional constituent of the brain (Crawford and Sinclair 1972). DHA or its precursors have to be provided in the diet. However, there is an order of magnitude difference in the preferential incorporation of DHA preformed into the developing rat pup brain ,as opposed to its synthesis from α-linolenic acid (Sinclair and Crawford 1972, Sinclair 1975). There is a paucity of DHA in the land food chain which also contains competing fats such as linoleic acid of the ω 6 family. The richest source of DHA is the marine food chain where it co-exists with the iodine and other trace elements vital for the development and function of the brain. There is also a paucity of iodine in the land food web with some 2 billion people today at risk to deficiency and consequent mental retardation in the young.

Arachidonic acid is also a second major component of the brain. Of the two fatty acids DHA is the most difficult to synthesise and hence limiting. Arachidonic acid is largely of land origin but it is also available preformed in warm water sea and fresh water foods.

The movement in the 19th t0 21st centuries away from traditional use of sea foods and emphasis on land based food supply is a likely cause in the rise in brain disorders including mental ill health, stress and other psychiatric disorders now apparent.

With brain disorders having overtaken all other burdens of ill health in the West, a better understanding of DHA and its function could help motivate the required policy changes based on existing knowledge, so much needed to meet this grand challenge.

Darwin on Conditions of Existence.

During the writing of the "Driving Force"[1], David Marsh pointed out that in all 6 editions of Darwin's treatise on evolution he makes an important statement. He wrote that there are two forces in evolution, "*natural selection"* and the *"conditions of existence"*
Of the two, Darwin writes, the latter was "the higher force".

This recognition by Darwin is of the force of the environment. Indeed after finishing the 6th edition he spent much of the rest of his life looking for what he called "pangenes". These he thought would be the interface between the environment and the genes. Although neither he nor anyone else discovered pangenes we now know even by the evidence of a common sense view of the history of life on the planet, that he was correct. And of course we now have as proof. Darwin's pangenes are to be found in epigenetics[2], which is an apparent, heritable change in gene expression independent of an alteration in the sequence of DNA and usually induced by an environmental or nutritional influence. The epigenetic change may even be stably maintained (Youngson and Whitelaw 2008) and operate over several generations with the appearance of a genetic shift.

After Darwin, Weismann considered the "conditions of existence" was too close to Lamarck. So he cut the tails off unfortunate rodents and watched generation after generation of cutting that they still grew tails. From this experiment he concluded that " the conditions of existence" had no role in evolution. He then wrote a paper under the title of the *"All Sufficiency of Natural Selection"*. From then on, evolutionary biologists with but few exceptions, believed only in the force of "natural selection" or neo-Darwinism.

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[1] The Driving Force: Food , evolution and the Future Crawford MA and Marsh DE, 1989, Heinaman
[2] See A Handbook of Epigenetics, Elsevier, 2011.

Weismann should have known better that his experiment was one of "mutilation" not "conditions of existence". After all, the Welsh sheep farmers had been cutting off the tails of their sheep for centuries. Moreover, Professor Ephraim Yavin of the Weismann Institute for Science, in Israel, pointed out to us that it was even more surprising for a man with a name like Weismann to indulge in such mutilation when the Jews had been cutting off foreskins for 3,000 years! The Egyptians before that had been doing the same so the practice dates back for perhaps 7,000 years! Needless to say both Egyptian and Jewish new borns still produce foreskins.

Such an elementary misperception by Weismann was unfortunately accepted readily by the Victorians who saw themselves as a shining example of natural selection and the survival of the fittest in the way they were leading the world in the industrial revolution and colonisation of the planet.

It is important to recognise that Darwin frequently comments on the "modification" of species by natural selection which is quite different from their origin. Even within that framework, random mutation is now seen as an inadequate explanation for evolution, never
mind the origin of species. To explain origin, T. H. Huxley invited his readers to imagine monkeys randomly typing. They would eventually produce the works of Shakespeare. If a monkey hit 3 or 4 keys every second then to work with 45 keys available, and with the log of 45 = 1.65 the number of permutations is greater than a 50 figure number to produce one line of a Shakespeare sonnet! Even if the monkey started at the big bang he would struggle to get through the permutations within the life of the *universe*. This *reductio ad absurdum* is not an argument for intelligent design but an argument for the dominant role of the laws of physics and chemistry. The origin of life and evolution was not a random process. Hydrogen, the first and commonest element, does not react with gold but does with oxygen to produce water. Even then it will not do it at the temperature of a star. At very high temperatures' however, oxygen obviously reacted with silicone to produce rocks and then at lower temperatures with hydrogen to produce water. Making the chemicals of life is simply a more sophisticated business of the same principle. In other words the origin of life and evolution obeyed the natural laws in response to the "conditions of existence".

It is not difficult for us today to accept Darwin's wider view with the hind sight of last century. There was the increase in average height of about 0.4 inches/decade, a rise in cardio-vascular disease from a rarity to no 1 killer by the 1970s, and then obesity became a major concern of the first decade of this new century. These changes cannot be due to a change in the genome or natural selection. They are however, examples of the "conditions of existence" being the higher law. A geographically separate branch of H. Sapiens was changed in height, shape and disease pattern in one century.

There are four other stunning examples of the higher power of the conditions of existence.

1. The first is of course the origin of the solar system if not the Big Bang itself and its consequences. The Fermi Lab and the large Hadron Collider are examples of the seriousness with which physicists consider the conditions of existence.

2. The origin of life itself: the spark of life was followed by the anaerobic prokaryotes which existed for 2.5 billion years without change. The lack of change was determined by the conditions of existence as 2.5 billion years is ample time for many random genetic changes.

3. Change occurred when oxygen tension, excreted by photosynthesis

and the photolysis of water breached the Pasteur point at which oxidative metabolism becomes thermodynamically possible. When that happened about 600 million years ago, multi-cellular, air breathing systems evolved and all the 32 phyla we know today came into existence in a very short geological time span. No new phyla have been formed since.

4. The collapse of the Dinosaurs and evolution of flowering plants and mammals. Whether or not you believe in a meteorite catastrophe there was little doubt there was a change in conditions with the change in the primary producer, the plant life.

These episodes are just a few of many cited by Rattray Taylor (1983) and by Gould and Eldridge (1993) and described as "*punctuated evolution*". In each case it was the change in conditions of existence that marked each of these episodes. Natural selection undoubtedly played its part and would have streamlined the products. However, to emphasise the point, no amount of genetic change and natural selection had the power to change the life forms over the first 2.5 billion years of life on the planet. It was Darwin's "conditions of existence" exerting its all powerful effect.

The stalemate in conditions of existence over the 2.5 billion years of prokaryotes proves that DNA clearly could not change life itself no matter how "selfish" the gene may have been! DNA is remarkably stable. People even try to extract it from reptiles that lived over 60 million years ago! Nor is DNA changed in response to the small changes in temperature and pressures of the planet. The key to its success is the robustness of its stable reproduction. As the DNA ultimately dictates the proteins, the proteins themselves could not be responsible for change in response to different conditions. Hence something other than DNA must have responded to external change to explain the sudden explosion of cellular organisation, cell and phyla diversity in the Cambrian and for example the sudden change in size , shape and disease pattern in a segment of our own species in one century.

Traditionally it is considered that the birth of the 32 phyla was triggered by the advent of oxidative metabolism which is 8 times more efficient than anaerobic metabolism. This view is indisputable. As discussed above, within physiological temperature ranges, it is unlikely that a change in temperature or pressure would alter the DNA. However there is a feature in the biology of the cell that does respond to the environment, i.e. to temperature and pressure. That is , it does not show the robustness of DNA but is responsive to the both physics and chemistry of the environment. That feature is the lipid.

Lipids and the origin of multicellular life.

Lipids have a special relevance as they enter the biological picture at the Cambrian explosion with the formation of cell membranes, cellular and intracellular compartmentalisation. The next section will discuss the plausibility that they played their part on the sequence of events that followed the emergence of oxidative metabolism and indeed the Cambrian Explosion. The logical conclusion and importance of this insight, is that the lipids are still modifying our species today.

The life forms of the first 2.5 billion after the origin of life were anaerobic, single celled systems with no intracellular detail recorded in the fossil record. However, the Cambrian explosion was associated with the appearance of intracellular detail. The intracellular detail is provided by cell membranes which mean lipids. Hence lipid biology came into the picture to provide for the compartmentalisation within cells. This compartmentalisation is seen in every electron micrograph of a eukaryote cell (se fig 1).

The lipids formed the membranes that housed the transporters, ion channels, signalling and cell recognition systems. Lipids made possible, intracellular specialisation and hence cellular specialisation and then multi-cellular evolution. Thus lipids were key drivers in the Cambrian explosion.

Misconception of the cell membrane lipid.

For some time, people have given little thought to the lipids considering them as a barrier to water and water soluble substances. The text books and many research papers depict membrane lipids as a uniform, double row of match sticks with the heads facing the outside with the wooden sticks inside the bi-layer. They are drawn to look like a symmetrical railway track.

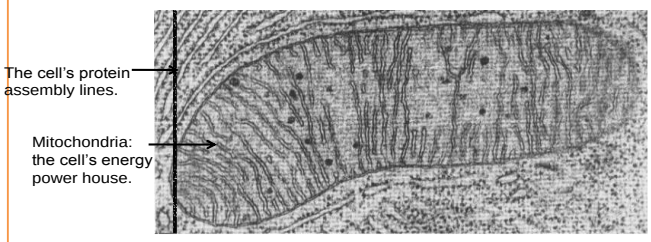
This view cannot be correct because the acyl groups which correspond to the sticks, vary in chain length mainly from 16 to 24 carbons. Acyl groups may be totally saturated and adopt a preferred straight-line, indeed like the match stick.

However there are many acyl groups with one double bond or more. The effect of the double bond is to kink the chain. Where there are multiple double bonds, the kinks impart a coiled structure. The range of 2 to 6 methylene interrupted double bonds in 18 to 22 and beyond carbon chains, alters the length, the space filling volume, electrical , physical and van der Waals) properties of the molecule

The polar head groups which are represented by the heads of the match sticks are not only of different shapes but range in charge strength from, for example, positively charged, primary amines to the powerful, quaternary amines associated with a negatively charged phosphate groups..

Fig 1: Lipid provided the intra and inter cell structure to create compartments and specialisation. They thus played a pivotal role in cell specialisation and speciation.

When oxygen became available in sufficient amount, complex molecules requiring high energy and oxygen were formed. Of these the lipids played an important role forming the cell membranes making intracellular compartmentalisation and specialisation possible.



Intracellular specialisation led to specialisation of the cells themselves and eventually speciation.

Moreover, the concentration of the quaternary amine phosphoglyceride on the external face of the cell membrane with the primary amine in the internal side immediately presents a dipole moment across the membrane adding electrical potential to the membrane.

How the misconception of the lipid membrane has been repeated from research papers to text books is difficult to understand as it so easily seen as false. Any one of these molecular arrangements completely destroys the regular match stick image of membrane lipids. The bi-layer seen in the electron microscope is a dead system not a live one. Unfortunately, this misconception has stymied the understanding of the specific properties of the individual molecular species of the lipids and the properties of the membrane as a functional unit with diverse electro-chemical and physical properties.

With regard to the physical properties, the melting points and hence the liquidity of the lipids varies from a saturated fat that is solid at room temperatures as in the beef fat people turned into candles before electricity, to a liquid with the introduction of one cis double bond in the Δ9 position, as in olive oil. Hence in the lipids, nature had building blocks for cells that could be used at different ambient temperatures as in the North Atlantic to the equator. The space filling and liquidity characteristics also enabled a response to pressure contrasts as on land compared to the Mariana Trench 10,911 meters deep. The

Panthalassic Ocean of the late pre-Cambrian 600 million years ago had 85% more water than today and any barren land above water was below the equator, down where the Antarctic is today. Hence the evolutionary process was taking place in sea water with varying conditions.

Lipid complexity advances sophisticated cellular organisation.

The study of the anaerobic systems of the rumen and gut flora show that the double bonds of unsaturated fatty acids are used as hydrogen acceptors resulting in saturated fatty acids and trans isomers. As the 2.5 billion year prokaryote period before the Cambrian explosion was anaerobic, it is unlikely that highly unsaturated fatty acids such as DHA with six double bonds, would have been in abundance. It requires 6 oxygen atoms to make the 6 double bonds alone. Also, the synthesis of phosphoglycerides themselves is energy intensive. Hence the emergence of oxidative metabolism made possible the synthesis of many types of highly unsaturated fatty acids and different phosphoglyceride molecular species.

There are 720 common molecular species of the phosphoglycerides without considering the variety of glyco-lipids, cerebrosides, gangliosides and the rest some of which, gangliosides included, offer not just structural complexity but also cell type recognition. This massive variety provided a huge diversity of molecular, physical and electro-chemical shapes to dock with the pre-existing variety of proteins in an optimal manner for function. It is likely that the proteins dictated the lipids first as the proteins had 2.5 billion years of evolution ahead of the sophisticated lipids

Cell specialisation in the Vendian and early Cambrian led to differentiation with the expression of different proteins which in turn led to a requirement for different lipids to fit with the cell type specific proteins. We now find that the membrane, lipid domains around the receptors, signaling systems, transporters and ion channels , are strongly conserved. This conservation is seen especially well in the fatty acid composition of the lipids associated with the rod outer segment of the photoreceptor and synapses. The membrane lipid in the cephalopods photoreceptor is virtually identical in all vertebrate species that evolved since. The vertebrates developed during the Late Cambrian, and diversified during the Ordovician period some 440 – 490 million years ago (Kroger 2008).

It is known that different cells have different global lipid compositions which mean that the differentially expressed proteins are taking advantage of this wealth of lipid diversity. The brain lipid is different from the heart. Mitochondrial lipids are different from the nuclear envelope. There are differences even within the mitochondria. And when you look deeper, you find even parts of the same membrane are different as in the rafts and caveolae compared with the region of lypophylic proteins with micro domains in evidence (Song et al 2006)

However, lipid-lipid interactions will also have played a role especially in the rafts and myelin. The influence of the protein on lipid structure decays logarithmically, with distance from the protein. However, in parts of the nervous system, there is so little protein lipid-lipid interaction will have to be a major determinant of composition. As in crystallization, it would be expected that like would form preferentially with like hence the uniformity of myelin where there is a lipid-lipid dominance. In the photoreceptor, where the number of polar head groups between rhodopsins is small the van der Waal and electrochemical influence of the protein stretches throughout the inter-protein space leading to a DHA rich, uniformity of composition at >50% of the acyl groups. There is virtually no species difference among the vertebrates and even some invertebrates.

Whilst it would be acceptable to conclude that the specialization and the emergence of the different phyla was driven by DNA and proteins, there must been a dominant role for the lipids in this process. The infusion of oxygen into the atmosphere was not just responsible for facilitating the higher energy efficiency of aerobic metabolism as is commonly thought. It was also responsible for this greater diversity of protein and lipid structures which were at the root of the emergence of cellular and subcellular structures and intracellular specialisation to be followed rapidly by cell specialisation and the 32 phyla.

The role of the fatty acids

Having seen the general significance of lipids what about the fatty acids that provide for much of the variability in physical and electrochemical properties. Examining the events in the light of modern knowledge, we now know about the function of the individual fatty acids as opposed to their function as a structural accommodation for membrane proteins.

For example, the Nobel Prize in Physiology and Medicine 1982 for Sune K. Bergström, Bengt I. Samuelsson, John R. Vane was given for their discovery of oxidative derivatives of arachidonic acid as intimate regulators of cell function at a specific locality, especially in eicosanoid response to injury with thrombogenic and inflammatory responses. Indeed Samuelsson published evidence of oxidative products of arachidonic acid, best known for their thrombogenic and inflammatory properties in the response to injury. However Samuelsson also published the first evidence of an elegant symmetry of coordinating immune cell action to clean the damage and bring about the resolution of the injury through arachidonic acid lipoxygenase products (Samuelsson 1986).

The eicosanoids formed from arachidonic acid play important roles in neural function including sleep induction (PGD2), long term potentiation, spatial learning and synaptic plasticity (PGE2), resolution of inflammation (lipoxins). COX-inhibitors have been shown to reduce oxidative stress and cognitive impairment. Additionally, drugs which are used to treat depression have been shown to reduce the turnover of AA to PGE2 in the brain. Diets deficient in ω 3 PUFA lead to reduced DHA in the brain and increased turnover of AA to eicosanoids, an effect which is overcome by restoring the ω 3 PUFA to the diet. In neural trauma and neurodegenerative diseases, there is a dramatic rise in the levels of AA-derived eicosanoids (Tassoni et al 2008).

In addition to the cyclic and oxidative products of arachidonic acid there are also oxidative and anti-inflammatory products of DHA with neuroprotective bioactivity (dihydroxy-docosatriene, neuroprotectin D1) which are strongly neuroprotective (Lukiw et al 2005, Bazan 2009). Moreover, the highly unsaturated fatty acids in the membrane phospholipids can act on their own. They can be released and act as ligands of nuclear receptors, controlling certain genes (Chawla et al 2001). Arachidonic acid itself is a ligand for the PPARS and DHA for the Retinoid X Receptors (de Urquiza et al 2000) and will switch on over 100 genes involved with brain development (Kitajka et al 2004).

The impact of maternal ω 3 deficiency during rat fetal development illustrates the deprivation of neuronal migration and neurogenesis in fetal rats whose mothers have been deprived of ω 3 fatty acid and hence DHA in the fetal brain (Yavin et al 2009). DHA has also been shown to promote neurite growth and synaptogenesis in embryonic hippocampal neurons (Kim et al 2011). Moreover, the molecular species are distinct physiological membrane constituents (Brand et al 2010). Stearoyl-arachidonyl- di-acyl glycerol, which is specifically released in

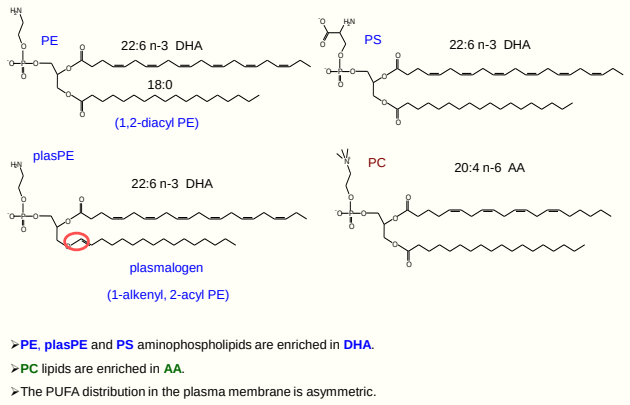
cell activation is responsible for the activation of Protein Kinase C (Hindenes et al 2000). Hence here is another dimension to the function of the lipids in which the lipids can be seen to contribute to cellular information, gene expression and functional regulation very much in response to the environment and local events with surgical precision.

The view we wish to put to the reader is that the complexity of the lipid molecular species which emerged under the first conditions of oxygen availability, offered a multi-dimensional sophistication of chemical, physical and electrical characteristics, to membrane structure critical in optimizing the function of the signaling systems and that of other specialized membrane bound proteins. That is, there was a Cambrian lipid explosion that led to structures, cellular and intra-cellular compartmentalisation and ultimately multi-cellular specialisation. Clearly, the lipids would have had an important role in the subsequent evolutionary events when there were serious environmental alterations. The evidence from molecular biology even supports the importance of DHA not just in brain development but also in the evolution of the brain itself. These factors would have operated in an epigenetic manner during cerebral expansion to form H sapiens.

The language of DNA operates with 4 letters for its words, with several words forming a sentence that eventually is translated into a protein. The proteins are built with 20 words that are assembled into a meaningful 3 dimensional structures. Because of the molecular movement of the final assembly of a protein, it is an example of supra-molecular chemistry.

A protein is capable of reversible non-covalent associations, hydrogen bonding, metal coordination, and electrochemical effects involving lipophilic and hydrophilic assemblies. Membrane proteins dock with the lipids which have similar non co-valent binding properties. The lipids however have a greater diversity of structures in their molecular species which provide the conditions for membrane protein function.

Fig 2: Some Key Brain Phosphoglyceride Molecular Species



- **PE**, **plasPE** and **PS** aminophospholipids are enriched in **DHA**.
- **PC** lipids are enriched in **AA**.
- The PUFA distribution in the plasma membrane is asymmetric.

There are a number saturated, mono-unsaturated and polyunsaturated fatty acids in the SN1 and SN2 positions of the phosphoglycerides that give rise to a large variety of fatty acid combinations within the phopsholipids in the membranes. For example there are choline, serine, inositol, and ethanolamine phosphoglycerides, plasmalogens, cardiolipin, sphingolipid and glycosphingolipid species which include the many galactocerebrosides found in neural tissue, and glucocerebrosides present in muscle and other tissues contributing to a considerable number of words in the lipid dictionary.

There are about 340 of the most common molecular species, 720 common and several 1,000 altogether if the rarer and sometimes trace amounts are counted. This system is operating in 6 dimensions with the 4th dimension: the electrochemical profile and the 5th Dimension: the van der Waals forces and the 6th dimension is temperature. This high degree of structural sophistication provides for the multi dimensional requirements for the physical and electrochemical environment for protein function.

It is now known that alteration of the lipid composition in the protein domains will

affect protein function. As the first point of contact between the environment and the cell is the plasma membrane we have here the explanation for the response of the cell and the genome to the environment. At the beginning of animal evolution, life was poikilothermic.

Hence the lipids would have responded to the temperature differences in contrasting habitats where there would likely also be contrasts in pressure. That would certainly have meant that the very most primitive life would have spread and found itself in widely contrasting environment with the different plasma protein domains at the least altering function and setting the stage for different evolutionary directions.

Table 1: FA species in *sn-1* and *sn-2* positions In addition to the sn-1 and sn-2 positions the sn-3 position (polar head group) can be substituted with either choline, ethanolamine, serine, inositol or glycerol giving rise to approx **720** molecular species.

sn-1 position	sn-2 position		
	monounsat	di-and tri-unsat	>/= tetra unsat
C14:0	C16:1n-7	C18:2n-6	C20:4n-6
C16:0	C18:1n-7	C18:3n-6	C22:4n-6
C18:0	C18:1n-9	C20:2n-6	C22:5n-6
C22:0	C20:1n-9	C20:3n-6	C20:5n-3
C24:0	C24:1n-9	C18:3n-3	C22:5n-3
C16ald			C22:6n-3
C18:0ald			
C18:1ald			
C18:2ald			

The present research priorities are pre-occupied with the genome centred paradigm. Whilst undoubtedly of great interest it is just possible that a greater contribution could be made by a shift in priority to the lipids good reasons for which we shall see at the end.

On genomic conservation and stability.

The function of DNA has dominated recent biology and unlike the lipids, is remarkably stable. The genome of the Puffer Fish (*Fugu rubripes)* was sequenced in 2001 (Aparicio et al 2002) (http://fugu.hgmp.mrc.ac.uk/PFW/Other/consortium.html), The regulatory elements of some genes such as the Hox genes (Suster et al 2009) and coagulation factors are strikingly conserved. Indeed, three-quarters of predicted human proteins have a strong match to Fugu although approximately a quarter of the human proteins had highly diverged from or had no pufferfish homologs (Aparicio et al 2002). The Puffer Fish genome dates back to 450 million years before now. That and much other similar genomic evidence implies a high degree of genomic conservation and stability. When the data on the human genome was published, Craig Venter the leader of the US Human Genome project declared that there was not enough to explain biological behaviour.

With the evidence today that the lipids do indeed influence gene expression, it may well be that they had a greater influence on these evolutionary events than they have been given credit. Remarkably, DNA can be extracted from long dead animals. However, that is not true of the highly unsaturated lipids which die rapidly with the death of the host. Phospholipase releases unsaturated fatty acids which are then peroxidised and destroyed. Controversial as it may sound, this gives the impression that the lipids are a life force more so than the DNA.

Docosahexaenoic acid in extreme lipid conservation over 600 million years

For the first 2.5 billion years of life photosynthesis converted sunlight into proteins and carbohydrates. At the beginning of animal evolution, DHA provided the basic membrane backbone of new photoreceptors that converted photons into electricity. The electrical and ionic consequences would have laid the foundation for the evolution of the nervous system and the brain.

If we date the conservation of DHA in signalling back to the dynoflagellate photoreceptor, we are talking about 600 million years of conservation. This conservation is despite the close precursor of DHA, the ω 3 docosapentaenoic acid (ω3DPA),

differs only by 2H, is less susceptible to peroxidation and requires less energy to synthesise (Bloom et al 1999). This striking conservation was despite genomic changes taking place from worms to humans. Hence whatever was happening in the nucleus, it did not (perhaps could not) swap docosapentaenoic for docosahexaenoic acid. This conclusion further emphasises the pivotal role for lipids in evolution. It is as though the lipids if not, then DHA was the master of DNA.

The phosphoglyceride DHA at the level of >50% is found in the photoreceptor membranes of the cephalopods, fish, amphibian, reptiles, birds, mammals and primates. Hence the conservation of DHA in the vision and the brain dates across the known range of the present genomic representatives of vertebrate evolution.

Fig 3 WHAT IS SPECIAL ABOUT DHA?
(WHY A 600 million year track record?)

CH3/\/\/\/\/\/\COOH DPA n-6
Δ-19 double bond missing

CH3\/\/\/\/\/\/\COOH DHA

CH3\/\/\/\/\/\/\/\COOH DPA n-3
Δ-4 missing

DPA n-3 THE Δ-4 DOUBLE BOND IS OMITTED
DPA n-6 THE Δ-19 DOUBLE BOND IS MISSING

Although the n-3 DPA is a precursor for DHA neither DPA replaced DHA in 500 million yrs of evolution . so these two double bonds may be critical to DHA's role in signaling membranes.

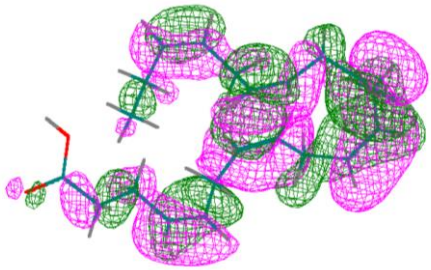
The difference in the composition of the brain lipids between species is not in brain chemistry but the extent or size of the brain reached by evolution in these different species (Crawford et al 1976). In the land mammals, the size of the brain relates to the availability of DHA.

The marine mammals have abundant DHA but difficulty in accessing arachidonic acid which they none the less need for reproduction and the brain (Caraveao-Patin et al 2009). Hence whilst on land DHA would be limiting, in the sea, arachidonic acid would be limiting.

DHA is clearly unique. Liquidity is often cited as the reason for DHA's special function but this property is little different from the ω3DPA. The liquidity differences between DHA and the ω3DPA do not explain the uniqueness of DHA over a 600 million years of evolution.

DHA appears to have special mechanical properties in curvature and springiness with Gawrisch et al (2003) providing clear physical evidence for its uniqueness (Mihailescu et al 2006, Soubias et al 2006).

Fig 4: Least Unoccupied Molecular Orbitals - LUMO in DHA (π bond energy different above and below planes; green lower, mauve higher energy).



π bond energy different above and below planes

In addition to what Gawrisch proposes, we speculate that the 6 methylene interrupted doubles bonds in DHA uniquely contributes π - electrons to signal transmission . Extended Huckel calculations based on the least occupied orbitals for DHA show that the bonds have a + and a - lobe and that the + and – signs of orbitals of the two different hydrogens on the CH2 groups also have + and – signs related to (typically opposite to) the signs of the adjacent π bonds (fig 4)..

This is a simple mechanism to explain electron coherence over a large distance, even though the double bonds are not extended resonance structures across a sequence of carbons with only single hydrogens. None of this works with DPAω3

which has five methylene groups following the double bond sequence. This idea offers a quantum mechanical electron transfer explaining precision of function unique to DHA and not able to work with a double bond missing at either end of the molecule (Crawford et al 1999).

The Cretaceous

The next obvious lipid involvement in the conditions of existence occurred during the Cretaceous as flowering plants evolved their protected seeds. They introduced into the land food web a novel, rich source of ω6 fatty acids. Coincidentally mammals evolved using the ω6 fatty acids for the synthesis of powerful adhesion molecules to capture the fertilised egg, and vascular development enabling placentation associated with the switch from egg laying to mammalian reproduction (Tassoni et al. 2008). Mammals require ω6 fatty acids where as fish require ω3 for reproduction.

The fish and reptilian era might well be expected to be based on green foods. The fish for example require ω3 for their reproductive process. However, the introduction of the flowering pants with protected seeds brought ω6 into the picture with the new mammals depending on ω 6 for reproduction. With the brain utilising ω6 and 3 fatty acids in a ratio of about 1 to 1 or 2 to 1 the injection of the ω6 to an already ω3 rich food web would have played a critical role in the advance of brain evolution that facilitated the larger relative brain capacity of the mammals compared to the previous reptiles and led to the cerebral expansion in human evolution.

There is good evidence to the competition between fatty acids especially between the ω 6 and 3 as they both use the same enzyme systems (Mohrhauer and Holman 1963, Budowski and Crawford 1985). Hence the emergence of abundant flowering plants with protected seeds can be viewed as another example of the changing biochemical conditions leading to an evolutionary novelty. Again an example of Darwin's conditions of existence.

Homo sapiens

The primate line that preceded H. sapiens separated from the great apes some 5-7 million years ago. Yet our genomes differ by only 1.5%. Thus our genome is adapted to wild food. Based on the notion that: "The Tissue us the Issue" the tissue of large land based mammals in which there was a universal collapse in brain size relative to the body, can be used as a judge of a balance of ω 3 and 6 appropriate for brain degenerate evolution or positive expansion and moreover the ability to synthesize DHA from the primary sources in plants. .



Fig 5 The rhinoceros gets all the protein it needs for a prodigious velocity of body growth reaching a 1 ton body weight in 4 years from birth.

The ratio within liver tissue for example in wild African herbivores, is about three ω 6 to 1 ω 3. In modern time, the ω 6 intake has been dominated by an increase in linoleic acid from the explosion in the use of soya, corn and sunflower seed oils (Blasbalg et al 2011). In the wild, marine mammals, the Dolphin comes the closest to H sapiens in brain/body size ratio. Here the ratio of ω 6 to 3 is close to 1 to 1. If however, we wish to use a marker of brain development, then DHA is the most limiting of the brain specific fatty acids.

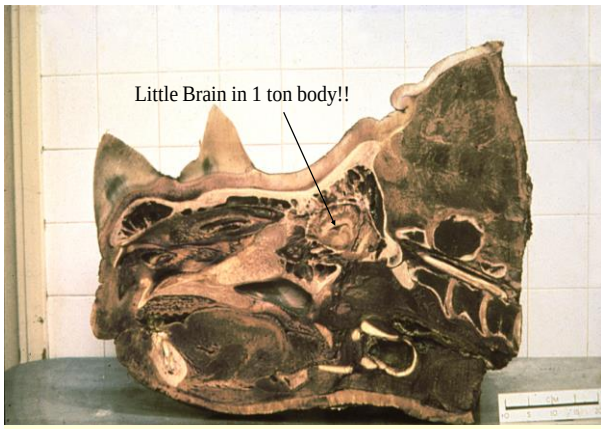
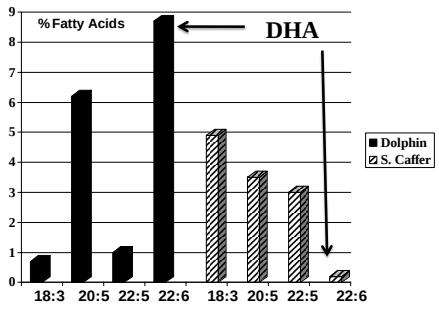


Fig 6: Despite such body growth and eating grass, a primary source of α-linolenic acid, it makesy little DHA and has a very small brain.

To obtain an idea of the optimal conditions for the brain, we can examine the ratio of linoleic acid to DHA. In the case of the Dolphin it is 0.067. In a typical large, savannah mammal it is 30 to 1 i.e. greater than a 400 fold difference in the tissue substrate pool which in the one case led to 1.8Kg brain in the marine mammal compared to only 350g brain in a similar sized land based mammal where linoleic acid was high and DHA was low.

Fig 7: Liver ethanolamine phosphoglyceride from Syncerus caffer (Cape buffalo) and Tursiops truncatus (dolphin)



This ratio makes the point that where tissue levels of linoleic acid are high and those of DHA are low as in the case of the Buffalo or Zebra, then you have degenerative brain evolution. By contrast when the linoleic acid is low and DHA is high you have cerebral expansion as in the case of the Dolphin. We suggest that the evolving hominid that became H. sapiens would have been more like the Dolphin chemistry than the land based mammals (Williams and Crawford 1987) . Note that the buffalo liver lipid is quite rich in α-linolenic acid, EPA and even the ω3 DPA but despite this wealth of precursor, fails to synthesise significant DHA (fig 7). The contrast with the Dolphin lipids in this respect is striking.

Coastal Evolution of Homo sapiens Would Provide the Evolutionary Advantage of a Rich Source of DHA not Available in the Land Food Chain and so Avoid the Loss of Relative Brain Capacity on Land.

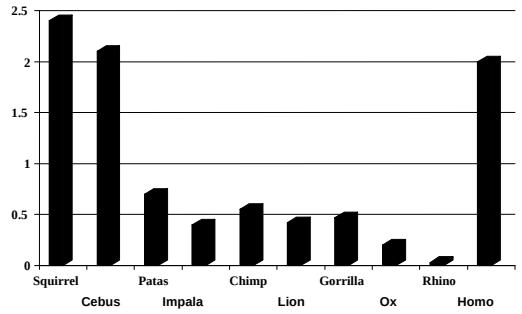
With clear evidence of the involvement of DHA in brain development, gene expression and function, DHA must have played a role in the evolution of the human brain. As the marine food web is by far the richest source, the evolutionary advantage of coastal evolution is obvious. On land, relative brain size degenerates as body size and growth velocity increases, from the >2% of small mammals (e.g. squirrels and capuchins) to < o.1% as in the example of the decline even within the primates from a cebus monkey to the chimpanzee, gorilla and rhinoceros (fig 8).

Starting some 50 million years ago some land mammals began to leave the land to radiate into the marine habitat. With unlimited access to the DHA food web, the marine mammals retained a far better brain body weight harmony. The dolphin for example has 1.8 Kg brain which compares to little more than 350g in a zebra which has a similar body weight. There is an interesting question as to what drove these land based mammals, wave after wave, into the sea?

Was it the DHA and happiness or a greater degree of consciousness? Consistent with the role of lipids in evolution, the Dolphin and the Gray Whale still retain their requirement for arachidonic acid assumedly for the mammalian reproductive process (Williams and Crawford 1987, Caraveo-Patin et al

2009). Hence whilst the marine mammals had an abundant supply of ω 3 fatty acids they were hard put to get their ω 6 arachidonic acid. The Gray Whale migrates 9,000 -11,000 kilometers from the Bering sea in the Arctic to the warm waters of the lagoons of Baja, Mexico where it breeds. A likely explanation for this huge effort is to seek out the arachidonic acid foods of warm waters (Caraveo-Patin et al 2009). None the less it is clear from the comparative evidence that both arachidonic and docosahexaenoic acids are required for the brain, and both are required by mammals.

Figure 8: Land based mammals compared to H. Sapiens.



By contrast. H. sapiens enjoyed coastal habitats rather than savannahs where all brains shrank. In this ecological niche, the evolving hominids would have had the best of both worlds. At just under 2%, H sapiens has a brain body weight ratio which would be totally exceptional if considered as a land based mammal but not if there was a rich supply of preformed DHA to maintain the harmony between body and brain growth as we evolved from a small primate to humans.

Logarithmic plots have commonly been used to obtain straight lines and explore the relationship between body size and brain size. Here the relationship is a straight line for most land mammals. This strategy of course means that one of the parameters is varying logarithmically to the other. In this case brain size diminishes logarithmically as body size increases. Even so the H. sapiens and the marine mammals do not fall on the straight line.

The conclusion is that on land, the rate limited synthesis from α-linolenic acid to DHA was outstripped by the velocity of protein accretion and body growth (Crawford et al 1969, 1993).

This evidence puts the evolution of H. Sapiens at the marine and lacustrine coastlines with access to preformed DHA from the aquatic resources. Fossil evidence for incontrovertible exploitation of the sea foods has been described in detail by Curtis Marean et al (2007).
"*We have identified the earliest appearance of a dietary, technological and cultural package that included coastal occupation, bladelet technology, pigment use and dietary expansion to marine shellfish, and is dated to a time close to the biological emergence of modern humans (160-180kya).*" (see also Marean et al 2010).

This evidence and the earliest identification of jewellery in the form of shell beads as necklaces (Bouzouggar et al 2007) and further back in time the population of the planet through migration out of Africa around the coast line (Stringer (2000), makes a compelling case for littoral origins of H sapiens

Physiological Evidence

Added to the biochemical evidence is the physiological basis first articulated by Sir Alistair Hardy (1960) and followed up by Elaine Morgan (1997, 2008). The basis of the Aquatic Ape Theory was simply that the physiology of H sapiens was more akin to that of marine mammals than those of the savannahs.

For example, we have a diving reflex, children are born knowing how to swim but have to learn to walk, bi-pedal locomotion would

have come naturally from wading, swimming and diving, we are hairless, we loose water by perspiration to keep cool and therefore "wherever we were evolving we had to have water to drink"[3].

All the savannah animals have hair and various physiological tricks to conserve water which is sparsely available on the savannahs. In 1961, Neil Casperd and MAC found they were loosing 1.5 litres and hour on a foot safari on the savannah in Uganda.

The Israeli army found they needed to drink 20 litres of water a day to remain fighting fit in the heat of the north African desert which would be very similar to our condition in the savannas of East Africa.

Iodine and selenium deficiency in inland populations strengthens the case of a coastal origin for the line leading to H. sapiens.

Adding the biochemical, physiological evidence to that of millennia of coastal occupation, fishing and boat building leaves little doubt of our coastal origins. The brain evolved in the sea. The DHA and indeed, trace elements such as iodine, zinc and selenium, were required for cerebral expansion inland all would have been sparse. That whole cluster co-exists in the marine food web. Keshan disease is considered to result from selenium deficiency found inland in China (Yang et al 2010).

Iodine deficiency has a spectrum of defects on the foetus ranging from retarded foetal development and brain damage to foetal death and stillbirths (Hetzel et al 1990, Mano et al 1987, Beck et al 2003, Levander et al 1997). Again, iodine deficiency is common in inland regions where 2 billion are currently at risk. It is seldom seen in the fishing villages. Correction of deficiency produces a "coming to life" writes Prof Basil Hetzel who coined the term iodine deficiency disorders many years ago. In view of the co-existence of iodine and DHA at their richest in the marine food web, it is highly likely that iodine deficiency is associated with an ω 3 deficiency, especially DHA deficiency! Nyuar et al (2010) report the lowest levels of DHA in the milk of mothers from the Sudan where there is a high prevalence of iodine deficiency (Izzeldin et al 2009)

The rift Valley: geological and paleontological evidence from the African Rift Valley and Nile basin

The East African Rift Valley is a unique tectonic province in both type and extent, unmatched anywhere else on Earth. The Red Sea, Gulf of Aden, and the East African Rift Valley are the only current examples of what is geologically termed a 'failed ocean'. Rifting began about 30 Ma, thinning and stretching the continental crust, but significant uplift did not begin until 15 Ma. The Red Sea axis has thin longitudinal strips of oceanic crust that are only about 5 Ma (Bohannon et al. 1989) (Fig. **4**).

In East Africa, faulting related to this crustal extension and uplift formed a series of half-graben basins, which link together to form the Rift Valley. Large lakes formed in these basins, with inputs from both interior drainage and river systems. On the border fault side of the lakes cliffs can rise to more than 2 km above the lake level.

Some lakes were so extensive during Cenozoic (65 Ma to present) that they are correctly termed proto-oceans. Lakes Malawi and Tanganyika presently have water depths of up to 1500 and 600 m, respectively. Many of the deep water channels are similar in form and scale to those observed in the deep ocean (Scholz et al. 1990; Leeder 1995;

[3] A comment made by Professor Philip Tobias at a McCarrison Society conference on "*Human Origins*", held at the Zoological Society 2006

Scholz et al. 2007). Lake Victoria is presently 69,000 km^2 and is the world's largest tropical lake (Stager et al. 1997).

East Africa has provided littoral environments on a massive scale throughout the evolution of *Homo*. *Homo* fossil and archaeological sites located within the East African Rift Valley (WoldeGabriel et al. 2004; Cunnane and Stewart, 2010) as well as other parts of the world are consistently and unarguably waterside areas replete with potential aquatic food resources (Bailey and Parkington 1988; Stiner et al, 1999; Klein et al. 2004).

Most or all *Homo* apparently entered Europe and Asia by moving northward along the Nile Basin into the Levantine and onwards (Bar-Josef 1992). While African *H. sapiens* dates to about 200 ka, the earliest known anatomically modern *H. sapiens* remains recovered outside Africa (93 ka) from Qafzeh, Israel (Stringer et al. 1989; Aitken and Valladas 1992) are associated with coastal habitation and consistent with migrations up and down the Nile corridor (Fig. 9).

Recently is has become evident that *Homo* made water crossings of the Bab El-Mandeb Straight from Eritrea to the Arabian peninsula (Derevianko 2009, Armitage et al. 2011, Petraglia 2011) (Fig. 9). Evidence for Middle Stone Age human occupation of the Red Sea coast of Eritrea dates to 125 ka, during the last interglacial (Walter et al. 2000; Bruggemann et al. 2004). Interestingly, Walter et al. (2000) conclude that "the eventual dispersal of humans out of Africa was due to increased human competition for marine resources, possibly during hyper-arid conditions."

This is diametrically opposed to previous savannah hypotheses, because littoral foods are now the driving force for a population migration, not an accidental or incidental food source. Eastwards, *Homo sapiens* made extensive water crossings to reach the Philippines by 67 ka (Mijares et al. 2010).

The number of individuals responsible for this migration is staggeringly small--perhaps only few hundred or thousand.

Numerous genetic markers in modern humans point to a recent African origin (DeGiorgio et al. 2009; Tishkoff et al. 2009). *At least some and perhaps all* of our ancestral *H. sapiens* survived in coastal refugia and thus were highly adapted to exploiting coastal/littoral environments and evidently benefitted tremendously

Fig. 9. Relief map of Afar Triangle East Africa, showing the Red Sea basin and initiation of the Rift Valley. Note also Nile Corridor to the Mediterranean region and Eurasia.

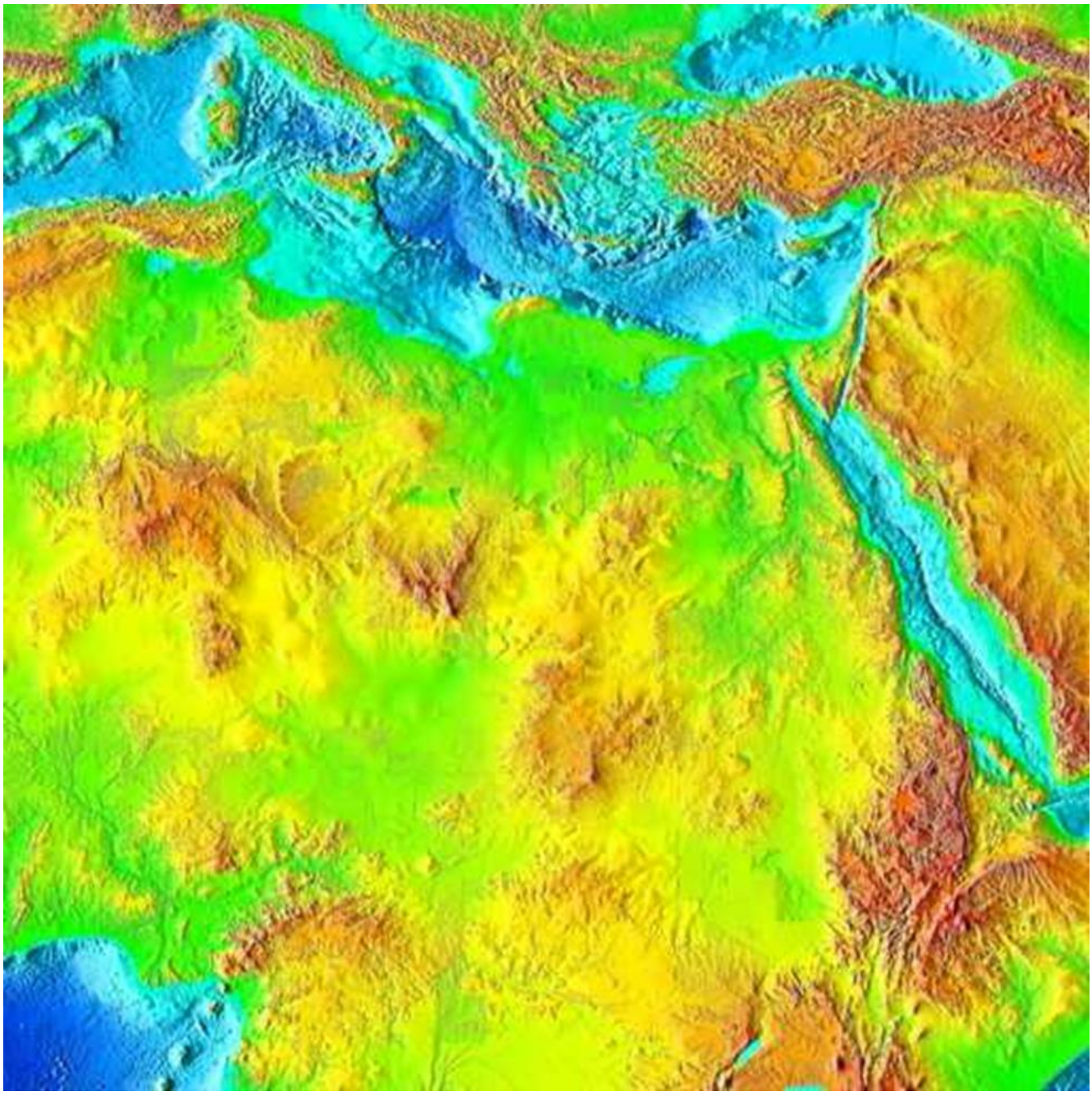
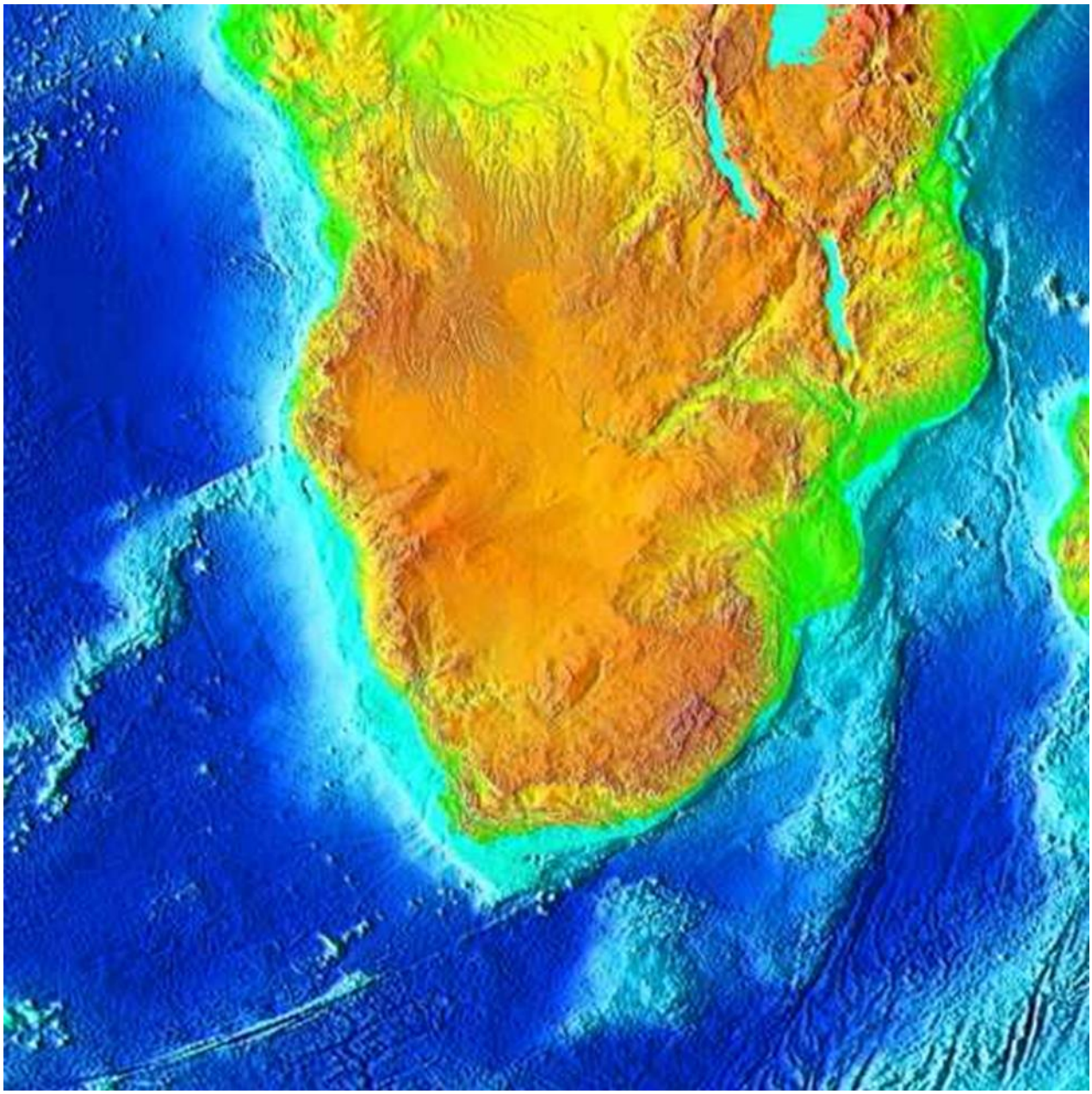


Fig. 10. Southern Africa, showing Cape of Good Hope and continuation of Rift Valley with its proto-oceanic lakes. Lake Victoria is on the northern border of the map. Note continental shelf on the southern border - this area was exposed during glaciation periods.



African coastal environments provide the first concrete evidence for modern human behaviour

There is virtually unanimous agreement that anatomically and behaviourally modern humans -left Africa to populate the entire world about 50 ka (Stringer and Andrews 1988; Klein 2008,2009; Tattersall 2008). The number of from exploiting this niche.

Tattersall (2008) notes that becoming human took place in two separate stages: first the distinctive human morphology became established in Africa about 200 ka, followed by symbolic behaviour 75-100 ky later in Africa, but at 40 ka in Europe. The complex human neural substrate existed as part of modern anatomy -but was not fully exploited until ***symbolic behaviour***

developed. The earliest evidence for human symbolic behaviour--the hallmark of modernity --comes from archaeological investigations of African Middle Stone Age humans. These sites are South African coastal caves filled with shell middens, fish bones, and the remains of marine birds and mammals, including cormorants, Cape penguins, fur seals and whales (Die Kelders, Klasies River, Blombos, Pinnacle Point, Ysterfontein . Associated with these assemblages are some of the oldest fossils accepted as modern human (Singer and Wymer 1982; Deacon and Deacon 1999; Rightmire and Deacon 2001; Schwartz and Tattersal 2005; Rightmire et al. 2006).

Recovered from Blombos cave (~75 ka) are decoratively engraved ochres and a precocious bone industry (including engraving) not seen in Europe until 40 ka (Henshilwood, Sealy et al. 2001; Henshilwood, d'Errico et al. 2001,2009; Jacobs and Roberts 2009). At Pinnacle point (~164 ka) Marean *et al.* (2007) found ochres and numerous examples of bladelet technology normally seen only in the Late Stone Age. At the same time, humans at Pinnacle Point used fire-treatment to improve materials use in stone work (Brown et al. 2009), demonstrating a significant engineering capability was present. Not to be overlooked are the precocious bone harpoon and fish remains in the Katanda lakeshore locality dating to 100 ka (Yellen et al. 1995).

The oldest known example of personal ornamentation consists of marine mollusc shells either drilled or carefully selected to be strung as a necklace. Some shells also have evidence for coloration with ochre. “Explicitly symbolic objects” such as shell necklaces are found at Blombos Cave (d'Errico et al. 2005), Grotte des Pigeons, Morrocco (Bouzouggar et al. 2007), Qafzeh and Skhul, Israel and at other locations in Morrocco and Algeria (d'Errico et al. 2009). Clearly these shells held value and humans either visited the shoreline or traded with others who had.

Numerous triggers may have played a role in the development of modern logical and symbolic reasoning and the shift to a primary reliance on cultural rather than biological evolution. Leading candidates include the development of language (Tatersall 2008), rapidly changing climate, and local increases in population that allowed ready transfer of cultural and technological concepts to peers and offspring (Mellars 2006; Jacobs and Roberts 2009; Powell et al. 2009). However, the outcome we observe around us today requires *as both a necessary and sufficient condition* that abundant LC-PUFA, as well as complete protein, trace elements, and vitamin sources be available to all members of a prehistoric society for generation after generation.

The most parsimonious means to do this is to assume that *Homo* palaeo-environments were consistently littoral marine, riverine or lacustrine. Interestingly, shoreline environments provide for the population increases that are indeed vital to keep cultural and technological innovations alive (Erlandson 2001; Marean et al 2007; Jacobs and Roberts 2009). These various aspects are not contradictory and indeed are interconnected.

Prior to the recognition that modern behaviour originated early in Africa as opposed to after 50 ka in Europe, most researchers looked to genetic mutation(s) which may have allowed the symbolic mind to appear. Now, considered fully are aspects of nutrition (Broadhurst et al. 1998, 2002; Cordain et al. 2001; Crawford 1992, et al 1999, Parkington 2003, Marean et al.2007; Cunnane and Stewart 2010), demographics (Powell et al. 2009; Marean et al. 2010) and language (Tatersall 2008). However, equally puzzling is the question of why modern behaviour apparently died out in Africa, then reappeared 30-60 ky later in Europe but not

in many places in Asia (Ambrose 1998; Deacon and Deacon 1999; Mellars 2006, Klein 2008; 2009; Powell et al. 2009; Patnaik and Chauhan 2009).

The fossil record is only 0f what people find where conditions allow preservation. However this 'mosaic' appearance of modern human behaviour as reported, is both easily understood and predicted by a model in which environmental factors strongly influence gene expression. Epigenetic changes in gene expression occur in only a few generations, and can result in (semi-)permanent changes in the organism that are passed on to offspring. While it may take several million years to evolve a complex primate brain, the 'switch' that turns it on to human cultural overdrive could happen in a hundred years. The influence of LC-PUFA alone upon gene expression is fundamental, dramatic, and profound (Chawla et al 2000, Kitajka et al 2002, 2004). Thus, if an entire local population has abundant DHA, I, Zn and Se in the food supply year-round and generation after generation, then the impact on gene expression would be predicted to quickly become more numerous, healthy, intelligent and technologically advanced *without any type of visible anatomical changes other than in brain development especially of the frontal cortex.*. Time after time, it is noted that identical anatomical features are associated with a wide range of tool technologies, puzzling researchers since the science of palaeoanthropology began. *This may not be confusion at all, but simply the influence of diet and environment on gene expression.*

Reason for Concern on the Food System and the Brain

In the above discussion we have tried to develop an understanding of DHA is the only ω3 fatty acid used in neural signalling processes over 600 million years, despite the large scale change in genomics over that same time period. John F Kennedy said "we celebrate the past to awaken the future". The evidence for the evolution of Homo sapiens as a coastal dweller, utilising the marine food chain is now very compelling compared to the image of a club and spear wielding progenitor on the dry savannahs of Africa. (Crawford 1992 , Leigh Broadhurst et al 2002). The brain first evolved in the marine environment utilising marine nutrients of which clearly DHA was a key for neural systems. It still utilises DHA today (Crawford 2007).

We now understand that maternal nutrition before and during pregnancy is an independent risk factor for low birthweight and poor pregnancy outcome (Doyle at al 1989, House 2000, Wynn et al 1994, Rees et al 2005, Brough et al 2010). Post-natal nutrition is also a priority to ensure good maternal nutrition for herself and for milk (Birch et al 2007, Uauy and Dangour 2009). Hence, poor maternal health and nutrition before and during pregnancy disadvantages fetal development resulting in low birthweight permanent mental and cognitive deficits (Litt et al 2005) with risk of heart disease, diabetes and stroke in later life (Barker 2007). Poor neurodevelopment restricts the individual's capacity to acquire numeracy and technical skills (Birch and Gussow 1970). In addition, in clinical trials, ω3 fatty acids protected against sudden death from heart disease (Marchioli et al 2002) . There is also evidence that a high linoleic acid diet will compete with the ω3 fatty acids inducing behavioural pathology (Fiennes et al 1973, Hibbeln et al 2004, Blasbalg et al 2011) and for deficits of marine fats linked to manic depression (Saugstad 2001). Depressed ω3 status has also been associated epidemiologically with Alzheimer 's disease (AD) (Beydoun et al 2007) . It is one matter to identify risk of AD and a completely different affair to attempt to correct such a process. Although many are trying to do treat AD in late life with ω3 fatty acids it is a tall order to attempt to challenge

a process so long in the making, possibly even before birth,.

The abundance of the oceans was so taken for granted that people are still hunting and gathering its products despite the fact that FAO informs us that the total world catch reached a limit 20 or more years ago. That hunting and gathering technique, is a technique rejected for land products by the fireside committee of 10,000 BC. Just over a century ago, oysters were gathered and presented on the bar table in the East end of London free for those who bought beer. In Maryland they harvested 616,000 tons of oysters in 1889 but only 12,000 tons in 2002. Porridge and kippers of Scotland have been replaced by a linoleic food as snap crackle pop. Those who know the chemistry of an oyster shell being mostly calcium carbonate, will recognise that in 1889 the landing of oysters removed 270,000 tons of CO2 in one year.

The challenge of the rise in brain disorders.

In the beginning of last century candles were made from beef fat a hard, saturated type fat. Then came electricity and we now eat the candles. Added to this dietary novelty was the hydrogenation of fish and plant oils to make cooking fats and margarines. Even worse the selection of livestock animals for weight gain, obesity and the use of high energy foods was amplified with intensification, growth promoters and denial of exercise.. A wild relative provides more protein energy than fat as would have been the condition throughout the adaptation of human physiology. The conventional, intensively reared carcass with 30% fat has 50% lean which translates into 9 times the calorific value coming from fat compared to protein. All of which ended up in stomachs together with added trans isomers from animal fats and hydrogenation of fish and vegetable oils . These were major features of the nutritional conditions which featured in the rise of heart disease from a rarity at the beginning of the century. A report by FAO-WHO in 1978 recommended a correction of this abuse of the animal but little has been done. Since World War II there has been an added nutritional change in the explosion of linoleic acid from soya, cereals and grains. In all of this the ω 3 fatty acids were swamped (Crawford et al 1988, Ghebremeskel & Crawford 1994, Blasbalg et al 2011).

First it was cardio-vascular disease that became the no 1 killer in the West. However, the heart and cardiovascular system is the first to appear complete in the human embryo. It takes shape and function to feed organogenesis. Hence brain development which consumes 70% of all the energy sent to the fetus from the mother in the last trimester is depednednt on the prior development of a heathy cardiovascular system. This sequence identifies the relationship between the heart and the brain

There is compelling evidence that the reasons are related to the increase in competing fats as described above, with loss of sea foods and their replacement by land foods First was the foods increasingly rich in saturated and trans isomer fats and more recently especially rich in linoleic acid (Hibbeln et al 2002, 2004, 2007). The rise in death from heart disease to be no 1 killer by the beginning of the 1970s, was considered to be due to “bad fats” . Having found that the brain is largely made of good fats (Crawford and Sinclair 1972), it followed that unless something was done, the brain would be next: a prediction published by Crawford and Crawford (1972). This position was acknowledged at the FAO-WHO first consultation on the role of dietary fats in human nutrition (FAO 1978) which identified essential fatty acid requirements for the brain and early human development and recommended the correction of the fatty food system. Nothing was done and if anything matters have got worse .

This prediction has been proved correct. Brain disorders now account for the highest cost in the burden of ill health in Europe at a cost of €386 billion for the 25 member states at 2004 prices (Andlin-Sobocki et al 2005). In the UK. Dr Jo Nurse for the Department of Health estimated the cost of mental ill health in 2007 to be £77 billion, a cost greater than heart disease and cancer combined. The cost was re-assessed for 2010 at £105 billion in 2010[4]. This matter needs urgent attention. Evolution does not stand still. We have the knowledge to shape our own present and future destiny. As Admiral Carmona said at the outset, "we do not have time".

That history forces the realisation of the mistakes in food policy based on increasing physical growth of plants, animals and humans instead of considering the requirements for the brain. Clearly this century has to focus on the requirements of the brain which will include iodine and other trace elements also found at their richest in the marine food web. With the wild fish catch having reached a plateau, aquaculture for carnivorous fish must also reach a limit. That means to avoid degeneration of the brain we should agriculturalize the oceans.

Conclusion:

The biological priority of Homo sapiens is the brain. The brain is largely made of lipid with its origin in the sea 500- 600 million years ago. Brain development is the province of the mother with 70% of the adult brain cells dividing before birth. Last century the nutrition paradigm for food, agriculture and human nutrition was based on protein and growth. This century a new and more appropriate paradigm is needed for Homo sapiens.

[4] Dr. Jo Nurse, Mental Health Division of the Department of Health, UK.

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