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Evolution of movement process as a key for human cognition.

Evolución del movimiento como clave para la cognición humana.

Evolução do processo de movimento como chave para a cognição humana.

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ABSTRACT

Movement is defined as a complex event in both the evolution of species and human development, which involves genetic and epigenetic mechanisms. It is linked with memory, attentional and linguistic processes, and it is required to create and use tools, defined as an extension and externalization of human hands, or the motor organs or effectors, so we believe is the basis of human cognition. The process created a parietal plasticity when incorporating tools into the body schema, which gave place to brain expansion by tool-use training. This sequence is considered relevant to the Homo sapiens development, and produces such level of sophistication to every cultural expression, that makes movement an important process both phylogenetic and ontogenetically.

Under this context, this article covers the evolution

RESUMEN

El movimiento, desde la perspectiva evolutiva, es una necesidad de las especies para sobrevivir sobre la faz de la tierra, que involucra mecanismos tanto genéticos como epigenéticos, vinculados a los procesos de memoria, atención y lenguaje, necesarios para crear y usar herramientas, empleadas como extensión de las manos humanas y de los órganos motores o efectores. Esto creó una plasticidad parietal al incorporar herramientas en el esquema del cuerpo, y dio lugar a la expansión del cerebro mediante el uso de las mismas y el aprendizaje de cómo usarlas. Esta secuencia se considera relevante para el desarrollo del Homo sapiens, y convierte al movimiento en un proceso filogenética y ontogenéticamente importante.

En este contexto, este artículo cubre la evolución del movimiento como proceso. Comenzando con las

RESUMO

O movimento, desde a perspectiva evolutiva, é uma necessidade das espécies para sobreviver sobre a face da terra, que envolve mecanismos tanto genéticos como epigenéticos, vinculados aos processos de memória, atenção e linguagem, necessários para criar e usar ferramentas, empregadas como extensão das mãos humanas e dos órgãos motores ou efetores. Isto criou uma plasticidade parietal ao incorporar ferramentas no esquema do corpo, e deu lugar à expansão do cérebro mediante o uso das mesmas e a aprendizagem de como usá-las. Esta sequência se considera relevante para o desenvolvimento do Homo sapiens, e converte o movimento em um processo filogenético e ontogeneticamente importante.

Neste contexto, este artigo coloca a evolução do movimento como processo. Começando com as

of movement as a process. It begins with the first molecular actions to create a mechanism to retain energy and metabolize food. Additionally, this article explains: 1) how motility opened a door to the evolution of species, 2) how actin gets an important role in the cytoskeletal support, and 3) the development of the skills that allowed them to survive. Lastly, we investigate the evolution of movement as an adaptation to the environment, and the design of a human brain capable of pushing not only every muscle to the limit, but becoming part of other systems as memory, language or attention, as part of the cognitive processes on humans.

Keywords: Movement; evolution; actin proteins; cell evolution; Central Nervous System development; cognition; Memory; Language.

primeras acciones moleculares para crear un mecanismo capaz de retener la energía y metabolizar los alimentos. Además, este artículo explica: 1) cómo la motilidad abrió una puerta a la evolución de las especies, 2) el papel de la actina en el apoyo al cito esqueleto, y 3) el desarrollo de habilidades que permitieron la pervivencia de las especies. Por último, se investiga la evolución del movimiento como adaptación al medio ambiente, y el diseño de un cerebro humano capaz de empujar no sólo cada músculo al límite, sino convertirlo en parte de otros sistemas como la memoria, el lenguaje o la atención, como parte del proceso cognitivo en los seres humanos.

Palabras clave: Movimiento; Evolución; Proteína actina; Evolución celular; Desarrollo del Sistema nervioso central; Cognición; Memoria; Lenguaje.

primeiras ações moleculares para criar um mecanismo capaz de reter a energia e metabolizar os alimentos. Ademais, este artigo explica: 1) como a mobilidade abriu uma porta à evolução das espécies, 2) o papel da actina no apoio ao cito esqueleto, y 3) o desenvolvimento de habilidades que permitiram a sobrevivência das espécies. Por último, se investiga a evolução do movimento como adaptação ao meio ambiente, e o desenho de um cérebro humano capaz de empurrar não só cada músculo ao limite, mas o converter em parte de outros sistemas como a memória, a linguagem ou a atenção, como parte do processo cognitivo nos seres humanos.

Palavras-chave: Movimento; Evolução; Proteína actina; Evolução celular; Desenvolvimento do Sistema nervoso central; Cognição ; Memória; Linguagem.

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“Nature is ever at work building and pulling down, creating and destroying, keeping everything whirling and flowing, allowing no rest but in rhythmical motion, chasing everything in endless song out of one beautiful form into another”

John Muir

Movement process is a complex evolutionary feature that began long time ago even before eukaryote cells. Currently, cell movement is possible through different process, which can be a somatic, biochemical, diffusible or non-diffusible sign that can be detected by receptor proteins located on the cell membrane and spread by them through signaling forces to the cell (Ananthakrishnan and Ehrlicher, 2007).

This process is possible thanks to a precise and complicated network of genes, proteins, and enzymes while engages a boundless redistribution of the actin cytoskeleton, through three stages in most of cells. First, a cell pushes the membrane forward by standing and regrouping (growing) the actin network at its leading edge. Second, it follows to the substrate at the leading edge and adheres (discharges) at the cell body and posterior areas. Third, contractile energy, produced mainly by the action of the acto-myosin network, pulls the cell forward (Ananthakrishnan and Ehrlicher, 2007).

However, this process didn't begin working this way since the beginning of the nature evolution. At some early point of life on this planet, it was required the introduction of ATP as the universal energy, which was an important stage in bioenergetic improvement. ATP synthase is an enzyme that creates the energy storage molecule adenosine triphosphate. ATP is the most commonly used energy exchange of cells for all organisms. This act displacing acetyl phosphate, which is a compound related in taurine, pyruvate and hypo taurine metabolism (Sousa, Thiergart, Landan, Nelson-Sathi, Pereira, Allen, Lane, and Martin, 2013). However, even if ATP is found through ancestries, it is not the only one motor inside of individual cells. The most accepted justification for ATP's increase to become so important, it is because is a result of the substrate specificity of the rotor stator-type ATPase. This protein, is universal between cells as the sequencer (Thauer, Kaster, Seedorf, Buckel & Hedderich, 2008) of all biological energy in the form of ATP, and it is produced from chemiosmotic pattern, so it has as work to protect the separation from the inside of the cell to the outside, and the harnessing of that electrochemical gradient via

a coupling factor, as an ATPase of the rotor-stator-type, meaning it has a better chance to succeed and it was adapted by most of cells (Martínez-Cano, Reyes-Prieto, Martínez-Romero, Partida-Martínez, Latorre, Moya, and Delaye, 2015).

However, these machineries were recruited long before the modern eukaryote cell, because prokaryotes, the first alive organisms, were developed in a sheltered and chemically rich medium, with dissimilar ways to get energy in order to move. In this sense, protein kinase cyclic nucleotide-binding (CNB) domains were widespread in the prokaryotic world, so it is believed that they were an earliest draft that co-evolved beside the cAMP (adenylyl cyclase pathway) or, as a mechanism for translating the stress-induced cAMP as a second messenger into a biological reaction. There have been found some kinase domains in prokaryote cell, so it is accepted that both cAMP and cGMP domains could be functionally related in the evolution of eukaryotes to an EPK (Eukaryotic Protein Kinase), so they can be found, for example in all fungi (Taylor, Keshwani, Steichen, and Kornev, 2012).

Assuming that motility is a process required to get an integration of nuclear and other cellular functions as a bidirectional passage across the nuclear envelope, this of course requires that all tRNA, rRNA and mRNAs must be re-distributed, and since proteins required for DNA replication, transcription, transcriptional regulation, RNA processing and overall nuclear organization are only imported, since translation is cytoplasmic, (Wickstead and Gull, 2011; Koumandou, Wickstead, Ginger, van der Glezen, Dacks and Field, 2013; Blombach, Smollet, Grohmann, Werner, 2016).

Under this idea, it is necessary to understand how cells changed.

Motility: from Prokaryotes to Eukaryotes

There is not a consensus about how the first cells were originated, some data suggest that the eukaryotic cell could appear from a merger of two prokaryotes cells, but most compelling evidence specifically mention an

archaeal host and a bacterial endosymbiont process that could produce a new kind of nature item and may have led to the contemporary complex eukaryotic cell (Davidov & Jurkevitch, 2009).

Of course, that had to produce a number of new mechanisms to get energy, so it is possible to say that primitive eukaryote possible could become a predator with the ability to devour bacteria and archaea in order to get food, but eventually endosymbiosis would lead to the improvement of a mitochondria and chloroplasts, producing a complete new feature; however, two processes would be important to complete phagocytosis. First, the organism would have to disable its rigid cell wall, leaving a malleable plasma membrane that could be modulated to find and surround a prey.

Second, the organism of course needed a mechanism for projecting the membrane in a way that could easily engulf its prey. This would require a cytoskeleton capable to produce specific forces to open and close barriers. So even if eukaryotic actin cytoskeleton was able to generate a force on the membrane, it seems other two mechanisms were necessary, first a projection force produced by polymerization and second, a motor molecule to move the actin filaments and put them near each other or to a membrane (Cox, Foster, Hirt, Harris, and Embley, 2008).

Under this idea, if all this was possible, then the polymerization-based membrane protrusion process would be able to develop almost naturally as a result of actin assembly, while the add-on of contractile machineries involving other steps to evolve the set of motor molecules and actin-binding proteins (Wickstead and Gull, 2011). The problem with this idea, is that some archaea and mollicutes do not have cell walls (Cavalier-Smith, 2002).

In this sense, eukaryotic actin-based process could possible developed microfilaments and tubulin- based microtubules, because some of the filaments of the bacterial cytoskeleton are essentially “*cytomotive*” which mean that they can produce movement without any assistance from other proteins, so filaments themselves can act as linear motors pushed by the kinetics of polymerization/

depolymerization process. That's why some researchers have explained that in eukaryotes, this activity increased the evolution of numerous classes of motors, as well as nucleators, severing agents, tip-binding factors, and (de) polymerases functions, while other cytoskeletal filaments appear to have a more indispensable function, offering opposition to external force or acting as a support to the cell (Wickstead and Gull, 2011).

Another hypothesis about how movement was possible in cells is called the *neomuran* hypothesis, which tries to explain the origin of archaeobacteria and its diversification. Cavalier-Smith (2002) explains it this way: “Archaeobacteria originated by two successive revolutions in cell biology: a neomuran phase shared with their eukaryote sisters followed shortly by a uniquely archaeobacterial one. The first, neomuran phase was an adaptation to thermophily and involved a really major transformation of 19 key characters, including replacement of the cell wall peptidoglycan murein by *N*-linked glycoprotein and a great upheaval in the cell's protein-secretion and DNA-handling machinery. The second, relatively minor phase of specifically archaeobacterial innovations, notably replacement of acyl ester membrane by isoprenoid tetraether lipids and of eubacterial flagellin by glycoproteins, involved further adaptations to hyperthermophile and hyperacidity, respectively. Substantially later, several lineages independently readapted secondarily to mesophyll. Lateral transfer of genes from the immensely older and far more diverse eubacteria often played a role in these secondary returns to mesophyll and may also have done in the origins of archaeobacterial hyperthermophily, sulphate reduction by *Archaeoglobus* and methanogenesis. Under this perspective, the origin of the first eubacterial cell could be 3700 million of years ago, with peptidoglycan walls and photo- synthesis, and the origin about 850 My ago of the ancestral neomuran cell, when *N*-linked glycoproteins replaced peptidoglycan and the pre-eukaryote neomurans evolved phagotrophy, internal skeletons and the endomembrane system” (Cavalier-Smith, 2002, p: 17).

With this in mind, cell origins have been explained with other two major models; first a fusion model where an endosymbiosis event distributing the mitochondrion came very early, or a fusion later model where endosymbiosis happened after development of several intracellular structures. Although the second model places accent a prerequisite for phagocytosis-like mechanisms to be present to facilitate endosymbiont acquisition which is considerate the origin of the eukaryotic cell and represents one of the fundamental evolutionary changes in the history of life on earth (Gray, 2012).

Over time, the host archaeon enlarged its area to relate with symbiont (without phagocytosis) to obtain these superfluous products. At that point, the host-symbiont coordination could exist in anaerobic and aerobic environments (Stairs, Leger and Roger, 2015). This proto-eukaryote had an archaeal cytoplasm and a hydrogen- produced an organelle also capable of oxygen-dependent respiration. Later, after the major lineages of extant eukaryotes varied from the last eukaryotic common ancestor (LECA), and aerobic and anaerobic metabolisms were differentially absent in anaerobic and aerobic lineages, generating the variety of energy metabolism and the present-day mitochondrion-related-organelles (Martin, Müller, 1988).

At this point all these hypothesis, land on another ingredient to allow motility in cells, this is the structural and architectural properties of the cytoskeleton. So, it is important to define that the cytoskeleton is mainly contained into three polymer systems: actin filaments (Wickstead and Gull, 2011), microtubules, and intermediate filaments. Actin filaments have a long shape and are formed by thin fibers. They have about 8 nm in diameter and are the thinnest of the cytoskeletal filaments, and they are also called microfilaments. On the other hand, other types are microtubules, and they participate in a wide variety of cell activities, because they are protein motors that use the energy of ATP to provide the motion to cell. Lastly, exist intermediate filaments, that are small and dependent on substrate stiffness and indentation depth, their principal

function is structural (Lodish, Berk, Zipursky, et al., 2000), to reinforce cells and to organize cells into tissues and epidermal cells, which are composed largely of proteins (Jalilian, Heu, Cheng, Freittag, Desouza, Stehn, Bryce, Whan, Hardeman, Faith, Schevzov, Gunning, 2015).

Actin protein and its role in the cytoskeletal support

Talking specifically about the actin cytoskeleton function is worth to say that this is regulated by a plethora of actin binding proteins and specific signaling pathways. It is also controlled by a convoluted collection of over 15 diverse sorts of actin filament arrangements, which have been identified in metazoans and can literally being modify in both spatial and temporal intracellular distribution in response to physical and environmental stimuli (Lodish, Berk, Zipursky, et al. 2000).

Something remarkable is the fact that two filament-forming protein families, tubulin and actin, dominate the cytoskeletons of all eukaryotes (Satir, 2016). From a microscopical perspective, actin filaments are semi flexible polymers with $L_p \sim 17 \mu\text{m}$. They have a diameter of $\sim 7 \text{ nm}$, and they are constructed from dimer duos of globular actin monomers, with a polar functionality; this means that they have a fast and slow growing individual end (they are called the plus end and minus end separately). The minus end has a critical actin monomer concentration that is ~ 6 times higher than that the plus end ($\sim 0.6 \mu\text{M}$ and $\sim 0.1 \mu\text{M}$ at the minus and plus end individually). When the end of an actin filament is exposed to a concentration of monomeric actin that is above its critical absorption, the filament end binds monomers and grows by polymerization (Satir, 2016; Lodish, Berk, Zipursky, et al. 2000).

This mechanism is important because contrariwise, when the concentration of monomeric actin is below the critical absorption, monomers separate from the filament end, and the filament shrinks by depolymerization. Basically, by having these two different critical actin concentrations at the opposing ends of the filament, actin

filaments can flourish asymmetrically, so when the actin monomer concentration is between the two values, only the plus end matures while the minus end shrinks, in a back and forth dancing. This process, when the stretch of the filament stays nearly constant and the polymerized monomers inside the actin filament transfer motion forward due to asymmetric plus end polymerization, is known as *tread milling*, and this is a critical feature of how polymerizing actin filaments can generate force (Medina, Worthen, Forsberg, Brenman, 2008).

At the same time, it is worth to say that microtubules, are the strongest of the biopolymers, with L_p ranging from 100 to 5000 μm depending on the filament length, (Hightower and Meagher, 1986), and act as spirals that may be firmly packed into packages where all the helices are associated, and this arrangement is critical to movement process (Satir, 2016). After all, actin is a globular component of the cellular cytoskeleton and one of the most abundant cellular proteins in cells (Jalilian, Heu, Cheng, Freitag, Desouza, Stehn, Bryce, Whan, Hardeman, Faith, Schevzov, Gunning, 2015), and the best conserved eukaryotic protein (Satir, 2016) found from unicellular organism to plants, animals, (Siccardi and Adamatzky, 2016; Medina, Worthen, Forsberg, Brenman, 2008; Hightower and Meagher, 1986) and fungi (Roy-Zukav, Dyer, Meagher, 2015), so certainly the mechanisms involved and highly mature.

Of course a high level of efficiency mechanism is not easy to design, so it is not a surprise that 60 actin-binding proteins approximately, have been described in animals and of course, contribute in a hug number of vital cellular processes, such as cytoskeletal structure, conservation of cell shape, cell motility, cell division, endocytosis and intracellular transport, (Guljamow, Delissen, Baumann, Thünemann, Dittmann, 2012), vesicle and organelle movements, cytokinesis, muscle contraction, (Goodson and Hawse, 2002) modulation of a variety of membrane responses, translation of several mRNA species, and modulation of enzyme activity and localization within the cell (Monshausen and Haswell, 2013).

So, we can say that actin is a member of a larger superfamily of proteins (Thomas and Staiger, 2014), which acts as an expressway connecting diverse points of the cell applying molecular motors driven by filament assembly energies to transport proteins and organelles across the cell's limits (Yi, Huang, Yang, Lin, Song, 2016). As addition, the polymerization into filaments is a remarkable characteristic, which is the basis of functional adaptability as result of an wide prevalence of actins in the living world (Bertola, Ott, Griepsma, Vonk and Bagowki, 2008).

Another important characteristic about actin, is the fact that is essentially regulated during cell migration, cell adhesion, cell division, and several other essential cellular functions, because actin is part of the configuration of many cellular structures including filopodia, lamellipodia, microvilli and stress fibers (Zhu, Zhang, Hu, Wen and Wang, 2013).

Such level of regulation is possible thanks to a network design. Eukaryotes employ additionally more than 100 actin binding proteins (ABPs), generally falling in two classes with either actin monomer or filament binding properties. The several interactions of ABPs with actin are believed to be dependable for the evolutionary limitation on its arrangement, making it one of the best conserved proteins (Van den Ent, Amos, Löwe, 2001). Excluding conventional actin, eukaryotic cells similarly contain actin-like (ALPs) and actin-related proteins (ARPs), which have well-characterized functions in cytoskeletal processes (Ventecinq, Jamieson, Meruelo, 2011).

Until now, six primary actin isoforms have been recognized in superior vertebrates, (Goodson and Hawse, 2002) and arthropods, (Brunet and Arendt, 2016; Monshausena and Haswell, 2013). being alpha-skeletal (ACTA1), alpha-cardiac (ACTC1), alpha-smooth muscle (ACTA2), gamma smooth muscle (ACTG2), beta-cytoplasmic (ACTB) and gamma-cytoplasmic isoactin (ACTG1). Moreover, actin can be organized in three pairs: two isoforms expressed in striated muscle (skeletal and cardiac tissue), two isoforms from smooth muscle (alpha-

smooth muscle predominately in vascular tissue and γ -smooth muscle in the gastrointestinal and genital tracts) and two cytoplasmic isoforms (Bertola, Ott, Griepsma, Vonk and Bagowki, 2008; Murrell, Oakes, Lenz & Gardel, 2015).

As complex and it can look, actin exists predominantly in one of two forms: monomeric actin (called G-actin) and filamentous actin (called F-actin). The interaction alongside these two actin systems is closely controlled by a specific collection of proteins that bind actin directly or indirectly. For example, Actin Depolymerizing Factor (ADF), also known as Cofilin represents one actin-binding protein that can strip actin by splitting and depolymerizing actin filaments (Bertola, Ott, Griepsma, Vonk, and Bagowki, 2008; Van den Ent, Amos, Löwe, 2001).

While the actin-depolymerizing factor/cofilin (ADF/CFL) gene family proteins have been associated in cellular processes from membrane and lipid metabolism to mitochondrial sustained apoptosis, a temporal-specific dividing of expression arrangements proposes that ADF/CFL protein variations have sub-functionalized but might have gained different functions during their evolutionary history. In this regard, some authors believe that mammalian CFL and ADF/Destrin have biochemical differences that are particularly recall functional divergence (Roy-Zukav, Dyer, Meagher, 2015).

Cytoskeleton

It is believed that “all living beings are in fact descendants of a unique ancestor commonly referred to as LUCA (the Last Universal Common Ancestor)” (Forterre, Gribaldo, Brochier, 2005), even if it's just a proposed life system that apparently was the progenitor of the three domains of life (Archaea, Bacteria and Eukarya), LUCA probably can explain why motility become so important to species.

In this regard, the eukaryotic cytoskeleton seems to have evolved from ancestral precursors related to prokaryotic FtsZ (which is a protein encoded by the *ftsZ*

gene) and MreB (which is a protein discovered in bacteria that has been documented as a homologue of actin) that show 40–50% sequence mainly across different bacterial and archaeal species, meaning after million of years is still around (Wickstead and Gull, 2011).

It seems that FtsZ is a plastid-derived and have a similar role in the division of the chloroplast and/or mitochondrion as in previous their free-living ancestors. So, it is assumed that FtsZ mediates prokaryotic cell division, and mitochondrial and plastid division in eukaryotes, by developing an energetic ring among potential daughter cells (or daughter organelles) (Koumandou, Wickstead, Ginger, van der Glezen, Dacks and Field, 2013).

Before cytokinesis, which is the physical progression of cell division, distributing the cytoplasm of a parental cell into two daughter cells, admitting two types of nuclear division called mitosis and meiosis. So, it is important to notice that mitosis and each of the two meiotic divisions result in two separate nuclei contained within a single cell (Cooper, 2000).

It's just a theory that cytoplasmic division of a cell was able to create mitosis and meiosis, deriving the common ancestor, so FtsZ was distributed to bacteria and euryarchaeal, but since it is found in almost all modern species and shows surprising plasticity in composition, with the core filament-forming proteins conserved in all lineages, the idea is highly suggestive (Forterre, 2005).

For the most part it is believed that FtsZ was also used for division in the youngest eukaryotic and later, it was involved as an actin-based machine for cytokinesis, and eukaryotic FtsZ experienced a radical change and it evolved into tubulin. Cytoskeletal proteins perhaps evolved even earlier, in the common ancestor of bacteria, archaea and eukarya, but FtsZ in particular is considerate an ancient protein, because FtsZ and MreB (which is a protein found in bacteria and identified as a homologue of actin) (Koumandou, Wickstead, Ginger, van der Glezen, Dacks and Field, 2013; Wickstead and Gull, 2011; Cox, Foster, Hirt, Harris and Embley, 2008), and it has seen that even ciliates contain actin, although ciliates are

microbial eukaryotes with two types of nuclei: a germline micronucleus (MIC) and a somatic macronucleus (MAC) (Faguy, Doolittle, 1998).

Of course, another important process that has had a very long evolution, is the control of actomyosin contraction, produced by an increase of intracellular calcium, which is a well-preserved mechanism capable to create mechanical stress in animal cells and underlies muscle contraction, cell migration, cell division and tissue morphogenesis (Poole, Lundin and Rytönen, 2015). Much of this complexity evolved before the last common ancestor of eukaryotes, meaning that probably, the distribution of cytoskeletal filaments situates limitations on the likely prokaryotic line made possible eukaryogenesis process, which is estimated to have occurred over one billion years ago (Wickstead and Gull, 2011).

It is hard to ignore that this crucial process in animal muscle physiology is an ancestral feature of eukaryotic cells (Tekle and Williams, 2016). However, it was necessary ATP to promote the rotor stator-type ATPase, explained before, so a protein that is as universal among cells as the code, and no doubt is an invention of the world of genes and proteins. After that, probably as Forterre (2005 p. 797) explains: "RNA played both the role of catalyst and genetic material and this could happen through several steps. After that, a new kind of cell began to have different needs while interacted with environment and eventually; actin was needed to allow new sets of skills". As a result, proteins as actin family and genes can be found within all phylogenetic trees, and some analyses show that actin genes could be divided into two major types of clades: orthologous group versus complex group. Codon usages and gene expression arrangements of actin gene copies were stable among the groups because of basic functions needed by the organisms but diverged within species due to functional diversification. In this sense, most vertebrates hold two genes for class IX myosins while in invertebrates, a single gene for class IX myosins has been classified. The two class IX myosins in mammals, myosin IXa (Myo9a, myr7) and myosin IXb (Myo9b, myr

5), subsist in diverse variations among species (Newman, 2016).

Since actin, myosin and calmodulin are virtually universally present in eukaryotic genomes, is important to study them separately. Myosin is constituted by a heavy chain containing the motor domain converting ATP-hydrolysis into mechanical energy along actin filament (with ATPase and actin-binding activities) (Newman, 2016), and usually a light-chain binding neck domain. In most myosin families, the light chains are calmodulin proteins; in others, specific calmodulin-related proteins have evolved, such as the essential and regulatory light chains of myosin II, while calmodulin is involved in the regulation of a number of intracellular processes, including cell proliferation (Luciano, Agrebi, Le Gall, Wartel, Fiegna, Ducret, Brochier-Armanet, Mignot 2011).

In other species, such as vertebrates, cytoplasmic actins look-like actins are present in many amoebas, yeast and slime molds, this is because invertebrate muscle actins are associated to vertebrate cytoplasmic actins more than to vertebrate muscle actin isoforms. It seems than actin isoforms particularly for striated muscle tissue first evolved in primitive chordates (Newman, 2016). Talking about early amphibians or stem reptiles, this gene maybe duplicated, which resulted in an alpha-skeletal and a modern alpha-cardiac isoactin. The smooth muscle isoactins are assumed to evolved during later development of warm-blooded vertebrates and likely originated from an early skeletal muscle actin. So far, over 30 different actins have been defined from diverse muscle sources, some of them are known by having a very specialized role (Faguy and Doolittle, 1998).

In this sense, when eukaryotic cells began to change external stimuli into membrane depolarization, and turn on triggers effector reactions, such as secretion and contraction, permitted to convolute a number of important and diverse cellular processes such as organelle movement, exo and endocytosis, nuclear transporting, and chromatin repair, so a variety of classes of actin binding proteins are found in plants and animals that

facilitate the vigorous nature that makes it one of the most dynamic characteristics in a eukaryotic cell (Murrell, Oakes, Lenz & Gardel, 2015).

So far, we can say that actin proteins family has a very important function to movement process, intra, extra and among cells. Being a very well conserved heritage from prokaryotes cells, there is no doubt that is a relevant part of the evolution of species. But, how did this happen?

Evolution of cells and movement processes

It accepted that life first began at least 3.8 billion years ago, around 750 million years after Earth was formed. Some theories claim that the first cell started by the insertion of self-replicating RNA in a membrane composed of phospholipids. It is known that these are the basic components of all the biological membranes, including plasma membranes in both prokaryotic and eukaryotic cells (Cooper, 2000), and how we have been exposing this lead to a dynamic strength for the evolution between prokaryotic, bacterial, archaeal, and eukaryotic cellular organization (Brunet and Arendt, 2016).

However, because cells required energy to move, the mitochondrion was likely the best mechanism possible, and it is well known for its function in ATP synthesis by oxidative phosphorylation. In this process, pyruvate from glycolysis is imported into mitochondria where it is oxidatively as decarboxylated to acetyl-CoA by Pyruvate Dehydrogenase (PDH) and becomes part of the Krebs cycle to produce nicotinamide adenine dinucleotide NADH, and Flavin adenine dinucleotide FADH₂, its function is to provide electrons to the electron transport chain. They both transport electrons by exchanging a hydrogen molecule to the oxygen molecule to produce water during the electron transport chain; these reduced cofactors link chemically with oxygen, by the electron transport chain (ETC), to produce a proton gradient across the inner mitochondrial membrane and finally reduce O₂ to H₂O (Stairs, Leger and Roger, 2015).

At the same time, the proton force drives ATP synthesis by an F₁F_o-ATP synthesis. However, in addition

to holding genomes that are replicated, transcribed and translated, mitochondrial process has an important function developing iron-sulfur (Fe-S) cluster generation (via the iron-sulfur cluster (ISC) system) as a biosynthesis process, since amino and fatty acid, phospholipid, vitamin and steroid metabolism are necessary to cells (Newman, 2016).

Given these points, in 1998, Martin & Müller, proposed the “*hydrogen hypothesis*” in which they discussed if eukaryotes could have risen across the symbiotic relationship of an anaerobic, strictly by hydrogen-dependent, strictly autotrophic archaeobacterium (the host) with a eubacterium (the symbiont) that was able to breathe, but capable to produce molecular hydrogen as a waste product of anaerobic heterotrophic.

In this regard, these authors explain the host's dependency upon molecular hydrogen, created by the symbiont, as the selective source that put-on the common ancestor of eukaryotic cells in motion. With this development, it is believed that the ancestor of mitochondria was an H₂-product, mainly by an anaerobic α -proteobacterium that had a syntrophic relationship with a hydrogen-dependent methanogenic archaeon, however, in an anaerobic ecosystem, the α -proteobacterium created ATP by the anaerobic extended glycolysis pathway, generating hydrogen, and of course it was necessary carbon dioxide and acetate as discarded products that were spent by the methanogen (Martin, Müller, 1988).

The selective benefit of these changes was the ability to remain producing acetyl-coenzyme A and eventually ATP from pyruvate (and/or malate) under hypoxic conditions usually encountered by free-living and anaerobic eukaryotic systems. However, with a need to adapting to new atmospheres, eukaryotes could acquire and express genes from prokaryotic or eukaryotic donors that permitted them to succeed (Poole, Lundin and Rytkönen, 2015), since it has both molecular and morphological attributes very conserved, they have participated as an essential role in the understanding of the origin and evolution of different eukaryotes (Tekle and Williams, 2016).

Besides the mitochondria, of course centrosomes are another old improvement. They are membrane-free organelles that serve as main microtubule systematizing cores in different eukaryotic lineages (Azimzadeh, 2014). In preparation for cell division, the centrosome duplicates during mitosis, so the sister centrosomes act as an important way to determine the indispensable bipolarity of the spindle. Because the role of mitosis is to divide a mother cell into two genetically identical daughter cells, the cell must guarantee that the centrosome inherited from the previous mitosis doubles once and only once (Sluder, 2014).

Such strategies are just an example of the multiple survival processes that evolution created with a range of delightful movement options. This is particularly interesting if it's seen in perspective, especially when we think that animals (Metazoa) are just one of some dozen freely developing groups of multicellular organisms. It is believed that they emerged more than 600 million years ago, including cells belonging to a bigger phylogenetic group, holozoa, which also involves some existing unicellular and transiently colonial systems (Tekle and Williams, 2016).

While plants, bacteria and virus are modest examples of motility, the transition from few cells organisms to vertebrates in water is a fundamental step in the evolution of terrestrial life, and the exponential expansion of bones and muscles became a very necessary item. Once animals left the aquatic environment, required a skeleton capable to resist the significant effects of gravity for example, as well as permit operative conduction of force to the substrate to allow propulsion, so it is not a surprise that in most terrestrial vertebrates, the bones of the appendicular skeleton provide this framework (Blob, Espinoza, Butcher, Lee, D'Amico, Baig, Sheffield, 2014).

As an example of this, a variety of actinopterygian fish species evolved to acquire the ability to navigate over land using combinations of fins that are prolonged by flexible bones. Some critical improvements to this evolution was the development of a weight bearing pelvis, hind limbs and their related musculature and movements that allow

running or walking back and forth, and probably this feature allow them to dominate in terrestrial locomotion. The fossil record exposes how the skeletal structure of the load-bearing limbs of tetrapods (animals descended from fish) has developed, but since soft tissues are not usually conserved as fossil evidence, so there is not clear evidence of how the dramatic alterations of the limb musculature started to change (Blob, Espinoza, Butcher, Lee, D'Amico, Baig, Sheffield, 2014).

No to mention that locomotor strategies in terrestrial tetrapods have evolved from the use of sinusoidal retrenchments of axial musculature, ostensible in ancestral fish species, to the dependence on powerful and complex limb muscles to provide propulsive force, this means the implementation of the fully derived mode of hind limb muscle formation from this bimodal character state is an evolutionary innovation that was critical to the accomplishment of the tetrapod transition (Cole, Hall, Don, Berger, Boisvert, Neyt, Ericsson, Joss, Gurevich, Currie, 2011).

Nevertheless, even if muscles, nerves and somatosensory processes are a big leap in evolution terms, a central nervous system was necessary to generate adaptive strategies. The origin of the nervous system was an evolutionary event that essentially changed how control is achieved within a multicellular body.

Nervous System: controlling the movement process

It is vastly accepted the assumption that the human brain weights in average 1.2–1.8 kg, and has around 100 billion neurons (Jékely, Kejzer and Godfrey-Smith, 2015). Although, it is believed that the origin of brain and central nervous system (CNS) can be marked by the Paleozoic era, 540 million of years ago (Strausfeld and Hirth, 2016), At the same time, it's believed that the origin and diversification of the animals occurred throughout the so-called *Cambrian explosion*, during a period when many important organ systems appeared (Kass, 2013). In this sense, the nervous system of humans must be considered the best draft in nature, not only among animals, but from

sponges, arthropods, chordates and placozoans (Budd, 2015).

As result of such a progress in nervous systems, early mammals developed from mammal-like synapsids over 200 million of years (Hejnal and Lowe, 2015). Synapsids are the dominant large terrestrial animals in the world, so they conquered the oceans like whales, pinnipeds and the air, for example bats, however they differed from mammals, as Kass (2008) explains, because they had “low-resolution olfaction, poor vision, insensitive hearing, coarse tactile sensitivity, and unrefined motor coordination, together with limited sensorimotor integration”

By the same token, evolutionary research has explained how such level of differentiation occurred, for example early mammals had tiny brains in comparison to their body size, at the same time, they exhibited considerably bigger forebrains, prominently expanded olfactory (piriform) cortex, a dorsal cap of neocortex, an expanded cerebellum, a thicker spinal cord, however these brains controlled simpler sensorimotor systems. There was also a good draft to auditory adaptations that would warrant high frequency hearing, and perhaps they could use high frequency communication calls, but later, mammals emerged from mammal-like reptiles about 200 million years ago and radiated into the over 3,500 living species (Collin, Davies, Hart and Hunt, 2009).

For this reason, some researchers believe that the relationship between distantly linked animals during the development of their central nervous system could lead the enlargement of a central nervous system with a distinct centralized medullary cord and a subdivided brain, since this is homologous across bilaterians, and then a morphologically and molecularly tri-partitioned brain connected to a central nervous system was developed in the final common ancestor of protostomes and deuterostomes, such idea also suggests a reduction in animals that have a much simpler organization of their nervous system (Bielecki, Høeg, Garm, 2013).

Important to realize, is that from a phylogenetic perspective, the typical debate of the origin of the nervous

system is whether or not it had one or more distinct origins. Yes, it is believed that nervous systems evolved once only, at the base of the so-called Epitheliozoa basically all of the animals separately from the sponges. However, the best indication for early nervous system remains the Ediacaran to Cambrian as a fossil record, but its complexity across species cannot be understood as increasing nervous system development, because an ecological aspect also seems to play a role in determining trace fossil morphology (Kass, 2013).

Under this context, it seems that motility has a distinct impact in human development (Dzib-Goodin, and Yelizarov, 2016), and species evolution, not only from a genetic, and cultural perspective, but also as developing cause to advance as specie, since movement is related with processes such as learning, memory and sleep, through many neurological networks shared for all these systems (Lotem and Halpern, 2012; Dzib-Goodin, Sanders, Yelizarov, 2017). These associations are important to cognitive skills and learning in order to help species to adapt to the environment.

Additionally, when we talk about the central nervous system, there are some considerations about the origin of sensory organs and how they could be important to brain evolution and movement process. In this regard it can be said that the origin of eyes for example, has dominated debates and theories about what selection forces have driven eye evolution; so it can be said that it was more than 540 millions of years ago when the first appearance of photosensitive receptors as single lens eyes and multifaceted eyes and their underlying circuits, not to mention that color vision evolved in the earliest vertebrates, providing the source for color perception in all extant vertebrate classes found today (Bielecki, Høeg, Garm, 2013).

With this in mind, it is important to understand the evolutionary limitations placed upon the shape, light reactions, spectral sensitivity and molecular assembly of photoreceptors in early vertebrates and their role in visual behavior, because paleontological evidence from the Silurian and Devonian periods shows that the lateral

eyes of the ancestral vertebrates were skilled to create image formation and rotate within their own orbits by seven extraocular eye muscles (Perrin, Sonnemann, Ervasti, 2010).

This means if all sensory systems react due to receptor adaptation, visual systems are not the exception. Also, since photo adaptation happens at a cellular level of photoreceptors it was an inevitable feature in metazoan vision. Thus, since photoreceptors adapt to constant visual stimuli and counterstrategies are necessary to prevent image fading or blindness. The best-known mean to prevent adaptation is the fixational eye movements in mammals (known as tremor, drift and micro saccades), which unceasingly refocus and renew the retinal image. These movements are produced by an oculomotor system and since they have a blurring consequence on the retinal image, additional neural adaptations in post-processing pathways have evolved to avoid the interludes of movement. These mechanisms are very powerful, but also very expensive in both energy and neural capacity, so they are not available for animals with less elaborate visual processing (Collin, Davies, Hart and Hunt, 2009).

Of course, it is not possible to forget the auditory system, which seems to be exceptionally sensitive to perturbations of cytoplasmic actins, possibly because actin is a key physical component of auditory hair cells, which transform sound waves to neural signals. Hair cells are contained in the organ of Corti, both of which feature a complicated architecture that is a requirement for appropriate function. The organ of Corti consists of three rows of outer hair cells and one row of inner hair cells, organized with several types of support cells. This ribbon-like structure goes longitudinally alongside the length of the cochlea. External hair cells improve sensitivity to sound, while inner hair cells are the auditory receptors. Both cell types are crowned with specialized structures called stereocilia, which are detailed microvilli made from a mixture of b-actin and c-actin filaments that are organized in a strongly bundled para-crystalline array (Chakraborty and Jarvis, 2015).

As a result of the specialized sensory motor systems, the nervous system enhanced the level of diversification. In this sense, it is worth to mention that the human–chimpanzee divergence is commonly estimated at 5–6 million of years however, some researchers consider this divergence could be greater than 7–9 million of years (Kass, 2013), meaning brain motor system could be used long before the human brain.

The primates brain evolution

There is no doubt that the density in skills and motor coordination of human brain is a highlight moment among primate's evolution. Only the neocortex constitutes about 80% of the human brain, and this is segmented into diverse specialized regions, this is only one reason that this brain like that mediates accomplishments and abilities has no comparison among any other species (Kass, 2013) and it is the reason for a unique adaptation in motor skills (Dzib-Goodin and Yelizarov, 2016).

Generally, the origin of nervous systems has been judged through two different theoretical models. Hashimoto, Ueno, Ogawa, Asamizuya, Susuki, Cheng, Tanaka, Taoka, Iwamura, Suwa and Iriki, (2013) call them the “input–output (IO) and internal coordination (IC) models”. The two models highlight two distinguishing features of the nervous system as a control device. These authors explain that IO models, have the main function to receive sensory information and process it to produce meaningful motor output.

As a result of such specialization, there is a difference regarding IC and IO roles, because they have two different functions: behavior, and also physiological roles, so it is possible to distinct three types of effectors that the nervous system can affect these: are cilia, muscles and glands. On the other hand, some physiological processes involved internal organization. In this sense, complex, muscle-driven physiological processes, such as peristaltic spasms that move the content of the stomach or heartbeat, require IC systems to switch them; while an

IO model tends to adopt an operational effector system, an IC model highlights the evolutionary change capable to produce new multicellular effectors. In particular, the use of large contractile tissues (muscle) by large organisms, is an important evolutionary development, since movement in a muscle is a challenging task that should not be taken for granted (Jékely, Keizer and Godfrey-Smith, 2015).

For example, ciliary pounding can be used for propulsion in an extensive range of small systems, but also has other uses. For instance, inside a sponge, cilia are used to allow water flow to permit access to food and oxygen, so the cilia must have coordinated movements, and this is a scenery in which an IC function influence can be relevant. Once a coordinated ciliary signal exists in an organism, other control strategies may adjust the activity of the cilia. Subsequently, cilia can become part of an IO system. In this sense a phototactic routing is an important IO function that is explicit to locomotion and can be found even in many metazoan larvae (Jékely, Keizer and Godfrey-Smith, 2015).

With a much more complex system, the brain of the genus homo could be developed in the early Pleistocene, just after 2 million of years. But long after, around 200 thousand years ago, the first draft of the Homo Sapiens can be recognized in fossil records. However, it's important to mention that the lack of fossils related to this period makes interpretation difficult, however some evolutionary patterns can be considered, for example the pelvises of early Homo, are similar in general about the shape to earlier hominids, and have traits that differentiate them from australopithecines, and it can be said that many of these traits are perhaps linked to modifications in locomotor performance (García-Grajales, Jérusalem, Goriely, 2017).

This is because in order to control so many new characteristics, the nervous system had to suffer an adaptive environmental influence. Since neuronal growth is a key process necessary to establish the neuronal network during neurogenesis, this could be consequence of all the new requirements that environment was demanding from brain. Besides its fundamental role,

neuronal growth also balances critical needs in human brain plasticity and neuronal renovation during all cycle of life (Kass, 2012a).

In order to warranty the process, numerous neurites from the soma, produce a highly dynamical hand-shape extensions called growth cones, this is a self-care process to human brain, and it can be found since early stages of neuronal development. This will continue growing, until one neurite specializes hooked on the axon, while all the other neurites become dendrites. This process was probable thanks to Paralemmin-1, which is a protein that stimulates cell development in plasma membrane. A family of these proteins can be found on vertebrates, and it has been possible the identification of paralemmin genes in the different vertebrate genomes, so it is believed they have a common gene organization (Khaltovich, Weiss, Lachmann, Hellmann, Enard, Muetzel, Wirkner, Ansorge, Pääbo, 2004).

The impact on this can be explained as a result of the changes in motility in neurons, particularly long neurites packed with G-actin need control the development of F-actin in reaction to dynamic events such as synapse structure or axon regulation through sensation of chemo-attractive/chemo-repulsive signals. Another key point is that the formation of ectopic F-actin need to be blocked to prevent physical obstacles that might obstruct vital transport roles inside these thin neurites and create damaging cellular results (Kass, 2004).

For example, it is known that neurites include a microtubule-rich cytoskeleton that offers a physical support to delivery both inside and outside directions for *cargoes* necessary to keep correct neuronal functions. So, in this regard it is necessary an energy-dependent molecular motor, including dyneins and kinesins, which are ATPases that physically assist sending targeted cargoes by directional motion lengthwise these microtubules. The kinesin superfamily protein KIF5 in particular is able to transport various cargoes involving membranous organelles, cytoskeletal proteins, and mRNAs (Khaltovich, Weiss, Lachmann, Hellmann, Enard, Muetzel, Wirkner, Ansorge, Pääbo, 2004).

This is particularly important to neurons, since once an axon found an area to establish, it will have to spread through spaces travelling across a rich chemo-mechanical signals, but it won't escape of complications until is able to locate its final reach-point, but physical forces will be acting, from molecular structures of the neuron organelles to the final formation of the whole organ. So, it is significant to notice that the main physical framework of the neuron, the cytoskeleton is an evolving active polymeric association that is actively participating in axonal outgrowth during a long period of time, in human brain (Kass, 2004).

Previously it was mentioned the F-actin and G-actin. Since the cytoskeleton is a product of evolution, this is constituted by three main kinds of filamentous polymers: F-actin, microtubules and neuro-filaments. Neurofilaments are inactive and apolar polymers. Although are the most copious cytoskeletal filaments in the axon, it seems they do not contribute during axonal growth. In contrast, the two other polymers, F-actin and microtubules, are really dynamic and polarized. "The old polymerizes at one end (barbed-end) by addition of G-actin and depolymerizes at the other end (pointed-end) by removal of monomers, while the latter polymerizes at one end (plus-end) by addition of tubulin dimers and depolymerizes at the other end (minus-end) by removal of monomers. While microtubules are the firmest cytoskeleton components and F-actin are less rigid on their own, the latter are able to build organized stiff structures thanks to the presence of high concentrations of crosslinkers. Their complicated interactions as well as their relations with the surrounding structures and associated motor proteins (e.g., Dynein or Kinesin for microtubules or Myosin II for F-actin) are crucial for proper axonal development, they also are heterogeneously dispersed along the axon domain" (Wickstead and Gull, 2011, p 515).

This gives to the cytoskeleton the capacity to respond in such vigorous way both mechanical or chemically and allow the development of so many arrangements, structures and *skills* that permit cells to performance the way they need into a specific background, during

growth and renovation as a key process in development of species and evolution in a higher standpoint (Dzib-Goodin and Yelizarov, 2016).

Through molecular motors, the cytoskeleton is able to get energy from ATP hydrolysis, transforming it into mechanical energy that can provide energy to the system into arrangements produced with not thermal motion alone. Beside with the characteristic shape of cytoskeletal filaments, which can assemble or disassemble quickly with chemical species gradients or regulatory signaling cascades, that allow to this nature item to respond in such particular way to the needs of cells (Popov, Komianos, Papoian, 2016).

However, it can't be denied that different anatomical brain structures developed at diverse times during vertebrate evolution, based on different needs of the environments and of course thanks to the new designs possible depending the kind of motion needed, and this produced the vertebrate brain known by its three divisions, with the spinal cord and brainstem (hindbrain, midbrain and thalamus) having more preserved constitution, maybe because it adapted to more dependable skills, and the telencephalon with a more varied organization, which exhibit three major structures, the pallidum and striatum having more well-preserved organization, and the pallium or cortex, with a more different organization. While the pallium is primarily hidden in mammals, it is typically nuclear in birds, reptiles and other vertebrates, mainly because needs over the environment are different in every specie. However, some changes happened with the appearance of the telencephalon through the invertebrate to vertebrate evolution, because diverse motions were required, denoting that the central nervous system has been an central target of selection (Khaitovich, Weiss, Lachmann, Hellmann, Enard, Muetzel, Wirkner, Ansorge, Pääbo, 2004).

At a molecular level, even if it has been accepted that more of those changes are due to Darwinian selection, that perspective was challenged by Kimura's neutral theory of molecular evolution (cited by Khaitovich, et. al, 2004). This theory is based on the vast differences seen in

nucleotide and amino acid sequences within and between species, that have no or only minor selective results. So now it seems, their incidence within a species and the fixation of differences between species are mainly the consequence of stochastic processes, meaning that are a collection of random adaptations (Kass, 2004).

This could happen in the middle of adaptations and deviation of species primates appeared around 80 million years ago, as a branch of the *Euarchontoglires superclade*. Kass (2004) explain that: It is believed they were short, arboreal, and nocturnal creatures; “they fed on small insect and vertebrate prey, buds, and fruit Primates constitute an order of mammals that is extremely diverse in brain size”. This branch particularly covered abundant lines of archaic primates that found extinction, and the branch euprimates that began to the current galagos, lorises, tarsiers, and the greatly varied anthropoid monkeys, apes, and hominids (humans and extinct species more closely related to us than chimpanzees), so they are in a considerate our common ancestor.

When Kass, (2012a) explains about the brain characteristics of this lineage, he says those brains were slightly stretched, but they don't have a big size and they have a similar proportion to body size than the brains of extant prosimian primates (lemurs, lorises, and galagos). “Their eyes were large, and frontally directed, and their temporal cortex was enlarged”. Consequently, it means that vision was important to survive in the environment, modifications for life in these branches of trees suggested that their neural systems for *eye-hand* coordination were well established to jump from tree to tree (Kass, 2012a).

It is accepted that the closest living ancestors of primates are “the Scandentia (tree shrews) and Dermoptera (flying lemurs) of the Archontan branch of Euarchontoglires”, while the more distant are the “Glires branch includes rodents and lagomorphs”. Although humans and chimpanzees are unrelated from a common ancestor by a few million years, human brains are three times bigger, and had maximum of that increase over the past 2 million years of hominin evolution. Only within thousands of years, human survived to their relatives,

mainly because a great ability to move, create with their hands and think. The youngest disputed hominin is the *Sahelanthropus tchadensis*, who lived approximately 7 million of years ago; so, there is no doubt that the emergence of the homo erectus sensulato in East Africa characterizes a fundamental turning point in hominin evolution (Maslin, Schultz and Trauth, 2015), and we still see their adaptation to the environment.

In this regard, the relative expansion of the cerebellum in primates besides to stereopsis and amplification of the visual coordination apparently reinforces primates fine viso-motor control and manual dexterity. This was particularly important, to search fruits and probably hunt, so this smooth-pursuit eye-movements in primates create a unique cortico-cerebellar pathway that evolved at the same time of foveal vision. “All major cortical regions, for example beyond motor cortex and including frontal and prefrontal areas, have reciprocal connections with the cerebellum” (Kass, 2013), giving a more precise movement process to stay alive and respond in the environment.

That's why Kass, (2012b) writes about: “these cortico-cerebellar loops form multiple, independent anatomical modules which are architecturally quite uniform”. And with such design, it was opened the opportunity to other fine movements, since generally speaking, some of the tools can be *used* for a different task. The best example of this is language process (Galván-Celis, Pechonkina, Slovec, Dzib-Goodin, 2015). The reason for this is that the unit of brains, the neuron, are not developed for a small or big brain specifically, but they will adapt their numbers and structure depending environment needs. So, reasonably rather than small brains developing small neurons, they will have less, and bigger brains will have more neurons, in this sense, additional growths in brain size could produce less and less gain to analyze and use information. A conceivable answer to why bigger brains become more modular by aggregating areas and subdivisions of areas in order to reduce the number of long connections (Hoffman, 2014), is that there is a relationship between energy consumption and the energy species get through their diet, based on general activity.

Of course, there were not only small other changes that made the human brain a better natural draft among species, lateralization for example, allowed to decrease the prerequisite for huge amounts of long, dense axons streaming through the two cerebral hemispheres motor cortex (Mendoza, Merchant, 2014), another action that must be added is the fact that in humans particularly, movement process is more focused on a super specialized digit movements, and of course, it means a specialization of ventral premotor cortex of the left cerebral hemisphere for speech (Khaitovich, Weiss, Lachmann, Hellmann, Enard, Muetzel, Wirkner, Ansorge, Pääbo, 2004), since this is a very elaborate skill.

This specialization, however didn't began with homo sapiens, early anthropoids showed many differences from other primates, and part of the reason was a cultural deviation, during 65–90 million years the diurnal niche eating fruit, buds, and maybe insect in the deadly areas of tropical forests, forced to an advance of posterior parietal sensorimotor cortex that involved areas like visual, auditory, and somatosensory in order to create a fine motor answer to the environment, and it is hypothesized than the frontal motor regions, as portions of a sensorimotor system, were increased and subdivided in early primate (Kass, 2008), this allows for human brains to create a different path and more specific and fine movements (Khaitovich, Weiss, Lachmann, Hellmann, Enard, Muetzel, Wirkner, Ansorge, Pääbo, 2004).

A good example of this process can be experimented with a very curious phenomenon, when something is touched with a single finger, can stabilize a person who is potentially losing his/her balance. This means the spatial perception of the fingertip is better distinct than the vestibular system and it is efficiently sensitive to detect small body change. Maybe because tactile feedback from the finger is basic for decreasing changing responses to the environment, but no effects of fingertip-contact forces on postural changes. An explanation is that bimodal neurons in the vestibular cortex reach the vestibular and somatosensory inputs might explain these effects on vestibular responses. But at the same time vestibular

cortex influence multimodal reference structures to maintain the unity of the spatial experience as a recall of the needs of the first primates in a complete different area, when they hand from trees (Barton, 2012).

That's why is understandable that when Homo Sapiens appeared, they were other motor behaviors controlled by the nervous system, and culture began to have an impact on the approaches to adapt to the environment, so it opens the door to cognition processes (Stout and Chaminade, 2012). So, it is logical to think that using tools perhaps allowed more exquisite abilities needed to survive, but undoubtedly is not the only one reason, because some other mammals use tools to get food, and by some reason didn't forced to those species to the level of human development.

Human brains: cognition and its relationship with motor control

Speech and the use of tools are both goal-directed motor actions (Stout and Chaminade, 2012). Now, the classical description of the tool is limited to external objects held by a hand in order to interact with the external environments, but modern humans also use tools to increase the reachable area or externalize our existing sensory organs, or to support the detection of information that is outside natural sensory range. This means that the natural intransitive movement becomes transitive, and this can create a "sense of the self (as the subject) and leading to the movement of ourselves or our body parts perceived as objects" (Iriki and Taoka, 2012).

But there are other tools, for example producing words and vocal learning, are a critical component of spoken language acquisition (Galván-Celis, Pechonkina, Slovec, Dzib-Goodin, 2015), since they are defined as "the ability to modify acoustic and/or syntactic features of sounds produced, including vocal imitation and improvisation" (Stout and Chaminade, 2012) and, similar than other motor activities, this implies implementation and comprehension of neural circuits integrating sensory perception and motor control, so they are linked as a need to survive and

communicate strategies, used into the environment (Iriki and Taoka, 2012).

Certainly, can be controversial the idea of language as a tool, since is easy to see a big difference between speech and the way a tool is used, especially because is clear that language is mainly a modality visual-auditory and the use of a tool requires visuospatial, somatosensory and manual skills, so the argument can be easily denied. But there is a good counter-argument, anatomically there are resemblances in the way speech and tool-use networks are systematized, including strong evidence of functional–anatomical intersection in inferior frontal gyrus and in inferior parietal and posterior temporal cortex. These discovers a similarity between cognitive processes and cortical networks that use speech and tools, and this explain why behaviors are best seen as special cases in the more general domain of complex, goal-oriented action (Stout and Chaminade, 2012).

Under this idea, it is plausible that the evolutionary intensification of tool-use could incorporate the combination of visual, and symbolic-abstract information leading to the appearance of a novel functional brain area for abstract understandings of tool functions, fulfilling the condition for the boost of complex human tool-usage (Hashimoto, Taoka, Obayashi, Hara, Tanaka, Iriki, 2013). This can be a good reason to explain why areas of the neocortex are especially big in the human cortex, for example the prefrontal granular cortex or language related Broca and Wernicke areas, which are considered as analyzers for integration of information from both sensory and motor areas (Galván-Celis, Pechonkina and Dzib-Goodin, 2014).

In this regard, Corballis (cited by Jablonka, Ginsburg and Dor, 2012) explains that motor control necessary to learning and teaching tool uses and fabrication, is the scaffold for the increasingly complex communication, emphasizing the role of motor control, arguing that the evolution of language could be originated by the control of manual and oro-facial gestures (and only later of vocalizations). That why Corballis proposed that the “voluntary motor control that was necessary for tool

making made gestural communication easy, and this was generalized to oral movements, which then led to speech”.

Another process that is not easy to ignore is motor imitation, which is a necessary ability to manufacture complex tools, observed among the Acheulean, and some think it was a prerequisite for the evolution of syntactic language, this because as Iriki and Taoka (2012), explain the recursive organization that adopts the combination of motor units is essential to design complex tools and at the same time, it is the basis of syntax, since message signs are inserted and merged into semantic representations giving order to every idea.

This is easier to understand because usually language can be divided into a conceptual–intentional system that deals with thoughts and meanings (Rakic, 2009), and a sensorimotor system that deals with the acoustic analysis of speech sounds and their production (Galván-Celis, Pechonkina and Dzib-Goodin, 2014), this implies that once a original cognitive demand, such as integration of motor tools into the body representation, has become implanted in the environment, adjustments of brain organization would be stimulated spontaneously within the normal developmental processes in subsequent generations. The incidence of such a plastic response during the lifespan as a result of behavioral modifications, could be possible by the existing of an adaptive capacity, and its subsequent consolidation (under selection acting on changing gene frequencies), as a default state that is unchanging over generations (Iriki and Taoka, 2012).

Eventually, other processes could be activated to use the motor areas that have changed as an effect of culture, and an example of this can be writing and reading processes, since they are *new* learnings in the history of humankind (Galván-Celis, Pechonkina and Dzib-Goodin, 2014).

Vocal control

Interestingly, vocal learning is a rare attribute into other species, so far it is recognized in only five remotely related groups of mammals (humans, bats, elephants,

cetaceans (dolphins and whales) and pinnipeds (seals and sea lions) and three distant related groups of birds (parrots, songbirds and hummingbirds). However, even if evolved independently those lineages of vocal learning birds and humans, both share clear forebrain pathways that control the understanding and production of learned vocalizations. In these pathways, all three avian lineages contain seven cerebral (telencephalic) vocal nuclei and several thalamic nuclei (Scharff and Petri, 2011).

These nuclei, are very well described in songbirds and parrots, and they are distributed between two sub pathways explained by Chakraborty and Jarvis. (2015) these are "1a): (i) the vocal production, or posterior, pathway that influences the production of learned song, which includes an arcopallium nucleus (songbird RA (robust nucleus of the arcopallium), parrot AAC (central nucleus of the anterior arcopallium), hummingbird VA (vocal nucleus of the arcopallium), analogous to the laryngeal motor cortex (LMC) in humans that makes a specialized direct projection to brainstem vocal motor neurons (MN), which in turn controls the vocal organs, the syrinx (birds) and larynx (humans); and (ii) the vocal learning, or anterior, pathway that is primarily responsible for vocal imitation and plasticity, which forms a pallial–basal ganglia–thalamic loop". This is equivalent to the loops found in mammalian brains that include Broca's speech area in humans, specifically ((Dzib-Goodin, Yelizarov, 2016).

Something remarkable to mention, is the fact that the song and speech regions in both pathways are inserted in or adjacent to non-vocal motor brain areas, and these non-vocal motor areas are present in other vertebrate species studied and could be involved in the learning process of non-vocal motor behaviors (Chakraborty and Jarvis. 2015).

There is no doubt that in this evolutionary scenario genes were important, and it has been said that the expression of FoxP2, which is a Fork head box protein P2 (FOXP2) is a protein that in humans specifically, is coded by the FOXP2 gene, and it is required for proper development of speech and language. During the evolution

of vocal skills, once the striatum got attached to other regions necessary for vocal learning to occur, FOXP2 mutated in humans and this might have affected neural transmission, and in Area X of the striatum, consequently became beneficial for sensory motor integration or defined timing of vocal gestures and to other motor learning tasks in adjacent non-vocal circuitry cells (Scharff and Petri, 2011). This would be a two-hit consequence of FOXP2 's role in language evolution, since if circuit changes, gene function changes in consequence to adapt to the new needs of the system (Galván-Celis, Pechonkina, Slovec, Dzib-Goodin, 2015; Galván-Celis, Pechonkina and Dzib-Goodin, 2014).

Tools manipulation

So, if language is linked with tools manipulations and design, in a way to change gene expressions, it is important to notice that primate manual manipulation, including those on skilled human that are capable to use a stone tool, have exposed three manipulative abilities studied as unique to the human hand. The first is precision control, defined as the ability to rotate and manipulate objects within one hand using the thumb and fingertips. While other primates characteristically need to use the palm as well or their other hand, a foot or the mouth to manipulate an object into the preferred position. The second characteristic is forceful precision gripping, in which the cushions of the thumb and one or more of the fingers are able to stabilize or control an object, and at the same time tolerate large external forces, such as when knapping a stone tool (Kivell, 2015).

In this sense, while other primates are enough skilled to control precision grips, typically tip-to-tip or pad-to-side grips between the thumb and index finger, these are not generally done with strong force, and this allow the third and uniquely human manipulative aptitude, which is the power to squeeze gripping of cylindrical objects, that allow fingers grip the object diagonally across the palm and the thumb, both wrapped around the object or in line with the forearm, for example when using a hammer (Kivell, 2015).

Of course, other primates are clever enough to control grips (using the palm) or diagonal hook grips (fingers usually stabilized touching the palm), but neither keep the same control that humans have to power squeeze grip. In this sense, maybe the most critical feature to the exclusive controlling skills of humans is our hand shape (comparative length of the thumb and fingers), and there is no way to forget the fifth digit, that is also exceptionally significant during stone tool-related behaviors, because the fifth digit stabilizes the leading hand during power squeeze grips and careful grips (e.g. during the strike of the hammer stone), or in precision grips of the non-dominant hand when maneuvering an object in the hand to find the desired position (Smouse, Focardi, Moorcroft, Kie, Forester and Morales, 2010).

However, all these skills improved over human development, lead to differences among cognition, as a process of interpreting and integrating information concerning the outside world, so it can be said that the perceptual information and the motor commands that represent the output of cognitive processes, are together in order to interoperate the surroundings. More recently, these distinctions have accepted that cognition is best conceived as a set of processes mediating the adaptive control of bodies in environments (Barton, 2012).

However, even if most animals are capable to recognize, recall and using information about the places they have been, this knowledge could potentially decrease uncertainty about the location and accessibility of resources, and even permit the anticipation of possibility of danger, thanks to memory features (Dzib-Goodin, Sanders, Yelizarov, 2017). However, there is not enough comprehension about how animals record and use spatial information, possibly a more realistic way or reinforced model for animal movement would accept the possibility of getting back to any earlier visited place even if such locales are outside the current perception area (Smouse, Focardi, Moorcroft, Kie, Forester and Morales, 2010).

This would mean that learning configuration of time and space is not easy, mainly because the process recruit many systems in order to manage data-acquisition

mechanisms to produce a specific output, since all that requires much memory and computation of specific information (Dzib-Goodin, Sanders, Yelizarov, 2017; Forterre, Gribaldo, Brochier, 2005).

So, it is important to realize that both cognitive and motor functions involve the learning of sequential actions. These sequences are adjusted with control by particular arrangements mediated by both executive function and automaticity, because learning complex sequences involves effective performance of executive processes, this have been demonstrated an overlap in the supplementary motor cortex and other brain regions, such as the cerebellum, basal ganglia premotor cortex, thalamus, ventrolateral premotor cortex, and precuneus, with increased activations at increased levels of complexity (Leisman, Moustafa and Shafir, 2016).

Other special feature associated with movement was the shift of body-space structure associated with the appearance of hominin bipedalism (Dzib-Goodin, Yelizarov, 2016), this might have another effect to development specific brain areas, and specifically extended to opercular cortex. Such neural development (construction of a neural niche) could enable the managing of abstract information, separate from actual physical limitation, by applying and re-using existing codes for spatial information processing to understand novel mental purposes (construction of the cognitive niche), and this could give as a result the development of language. This is believed because focused manipulation of the body image in space, demanded for tool use, would have rushed collaborating relations between the neural and cognitive niches, and because tool use needs a change of numerous bodily and spatial skills as well as logical and sequential relations of action components (Iriki and Taoka, 2012).

In this sense, tools engage cognitive brain functions, linked with fine movements, including language (Dzib-Goodin, Sanders, Yelizarov, 2017), since they were created one after another and shared into hominid environments as essential elements, that created what is known as construction of the ecological niche. Sooner or

later, a human-modified environment puts emphasis on following generations to familiarize to it, conceivably by getting additional resources for other relevant tissues.

Epigenetically this encouraged plasticity (including developmental or learning processes) so would contribute to allow that extra genomic information could be spread among generations via mutual exchanges between ecological, neural and cognitive domains of niches, which may have funded to hominid evolutionary processes. This scenario would find the human brain as part of an evolving holistic ecosystem (Iriki and Taoka, 2012; Godfrey-Smith, 2012).

Movement process and adaptation to the environment

Once tools and language began to interact to create better environments, were added more cognitive processes. It is accepted that after modern humans departed from sub-Saharan Africa, over 50 000–100 000 years ago, physical changes were necessary to diverse environments. In this regard, it is thought that when human populations were exposed to additional environmental changes, this produced cultural innovations, such as the increase of agriculture, which gave rise to new selective compressions linked to pathogen exposures and dietary changes and this at the same time, altered the frequency of individual adaptive alleles, so it is easy to believe that natural selection also make up the overall genetic and brain architecture of adaptive traits (Olson, Knoester, Adami, 2016).

From this perspective, other process was important, specifically animal-grouping behavior, which had important consequences for social intelligence and collective cognition, since grouping behaviors are persistent across all forms of life. As an example, is possible to mention swarming as a grouping behavior, where animals synchronize their movement with the rest of their group to maintain a cohesive unit. In this sense, swarming may increase matting success, spread foraging efficiency, or enable the group to resolve problems that

would be impossible to solve alone, plus there is indication of cerebellar development and participation in different cognitive functions, depending the kind of grouping behavior, suggesting a link between neocortex size and social group size (Barton, 2012).

Also, swarming behaviors could protect group members from predators in several ways, and in this regard, swarming can improve group vigilance, reduce the chance of being encountered by predators, and reduce individual possibility of being attacked, allowing an active protection against predators, or reduce reducing predator assault efficiency by confusing the predator (Olson, Knoester, Adami, 2016).

In other words, it is important to move efficiently into the physical space, alone or in group, in order to get a better opportunity to survive, and by this reason Darwin (cited by Kivell, 2015), first suggested that the introduction of bipedalism was directly connected to tool use as a way to free the hands and expand the locomotion. So, the relationship regarding motor function and cognition can be understood, in part, in the context of the evolution of human bipedalism, which helped as a significant basis for the evolution of the human neocortex as it is among the most complex and sophisticated of all movements (Jeong and Di Rienzo, 2014).

This gave humans a unique capacity to relate gravitational forces as a direct result of the existence of the erect position. The basis of the continuation of this genetic mutation is based on the notion that bipedalism had created larger pools of neurons. It is debated that the same evolutionary process has permitted to develop the binding of the motor system into synchronous, rhythmic, purposeful movement, which expanded to eventually allow for cognitive binding and perception (Leisman, Moustafa and Shafir, 2016).

This required a change for the hips and pelvis, not only in motion but muscle innervations (Dunbar, Horak, Macpherson, Rushmer, 1986), since walking and running implicate more support from joints and ligaments (Muehlenbein, 2015) and changes in knees as

a mechanical motor to use and produce energy to move erected (Hogervost, Bourna, & de Vos, 2009). So this adaptation provided a better synchronization and efficiency to hip extensor mechanism that create a different system comparted with other hominids (McHenry, 1975), that pushed homos from the arboreal walking to the ground (Hanna, Grabatosky, Rana and Schmitt, 2017).

This development allows humans to move further, and explore other ways to survive, like creating harborage, find different kind of food and be part of other groups. While memory of food locations and higher cognition may limit the benefits of random walk schemes (Dzib-Goodin, Sanders, Yelizarov, 2017), so called Lévy walks may have result from with the evolution of a hunting and gathering lifestyle in human lineages. Lévy walks are an unsystematic walk creating a new strategy used by a wide variety of organisms when searching for food (Raichlen, Wood, Gordon, Mabulla, Marlowe and Pontzer, 2014). This kind of search implicates frequently short move steps (defined as the distance traveled before pausing or changing direction) merged with unusual longer move steps (Smouse, Focardi, Moorcroft, Kie, Forester and Morales, 2010).

This movement arrangement can be essential to understand how humans perceive and interrelate with the world within a wide range of ecological frameworks, and it might be adaptive behavior to solve food distribution arrangements on the landscape. The widespread use of this movement pattern among species with great cognitive disparity insinuates a link between hunting patterns within different organisms, including humans (Raichlen, Wood, Gordon, Mabulla, Marlowe and Pontzer, 2014).

As a result of the interaction with environment, larger regions of posterior parietal cortex and frontal motor cortex become part of special networks dedicated to generating different series of movements, consequently, motor areas include primary motor cortex, ventral (PMv), and dorsal (PMd) premotor cortex, the supplementary motor area (SMA), and the frontal eye field (FEF). However, movement cannot do too much without the interaction with senses, so somatosensory regions incorporate the

four areas of anterior parietal cortex. As a result, primary motor cortex and dorsal and ventral premotor areas are well-known as cortical areas, and each of these areas has a somatotopic representation of minor activities of body parts (Kass, 2008; Kass, 2012b). Curiously, these areas are compromise in movement disorders such as apraxia (Murillo Duran, 2007).

Conclusion

This paper is just a brief and not exhaustive view of movement process as a key of evolution of species and human cognition, specifically from prokaryote to eukaryote cells to human cognition. Millions of years have been needed to draft more than one biology model of our specie.

From this perspective, movement process is not only important in large scale of the universe, since it keeps galaxies and planets in a perfect dance, but it has an impact into cells, in order to create a diversification of functions, adaptation and physical features.

One scenario explored is that phagocytosis could be a key to change the evolutionary rhythm of life, and actin proteins created new options to motility, that is why a globular major component of the cellular cytoskeleton and one of the most abundant cellular proteins.

However, It was needed still a long period of time before see a primitive nervous system, probably because the advance of the sensory processes, that beside motor behavior began to create the neuronal networks in the first nervous systems that is possible to appreciate among different species. As a result the human brain with a sensory motor system capable not only to understand the environment, but also manipulate its own resources to create adaptive answers to the environment.

Once that human brain was capable to recognize itself is physical space and time, walking create a cultural revolution allowing even more connections, and allowing memory to create marks to recognize the environment. Some believe thanks to the use of tools, communication began in other ways more than just calls, and this create

a cognitive niche to connect with the rest of the human.

We have explored in other articles that memory was result of movement, so of course explains why is so important to learning process. From psychological standpoint, several authors have claimed that movements seen as physical activity are important to learning process, but in our perspective, they are not capable to explain why this relationship is so important to human brains.

That is why this complex process must be seen from different perspectives, from microbiology, genetic, evolution, cultural, cognitive, clinic and even artistic point of view, and certainly each area has many more to say, because it is, from our perspective, very important to understand how cognition built human brains, that is just one example of evolution of species.

We deeply believe human brain is not the last draft of evolution, cognitive processes have been modulated based environmental needs and those changes that prove to be important over the population will become part of the repertory and structures of the brains. This is not a human design, but a species mechanism to survive.

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