Academic Journal of Science,
CD-ROM. ISSN: 2165-6282 :: 1(3):169–184 (2012)

ALZHEIMER DISEASE AND DNA CONSCIOUSNESS

John K. Grandy

Whitestone Consulting LLC, USA.

In previous works I have discussed DNA consciousness and defined it, in a general sense, as DNA having a degree of consciousness, which is supported by the interaction-based model of consciousness and the concept of interaction-complexity-consciousness (ICC). The second part of the theory of DNA consciousness is that through the process of the ICC DNA possesses the ability to give rise to higher degrees of consciousness that ascends from the level of the cell to the complexity of the human brain. Alzheimer Disease (AD) is an age-related disease that has a genetic component. Some AD genes have been identified- APOE-ε4, APP, PSEN1, and PSEN2- as well as others that are under investigation. These genes display a strong relationship to the development of AD. In this work I shall discuss the connection between AD genes and the process of neurodegeneration. I will then illustrate the relationship between the process of neurodegeneration to DNA consciousness and the ICC. In addition, new gene therapy involving the fibroblast growth factor-2 gene (FGF-2) have been shown to reverse the memory impairment in mice with AD, which I will use as further proof to support the emerging science of DNA consciousness and it's connections to neuron-based consciousness.

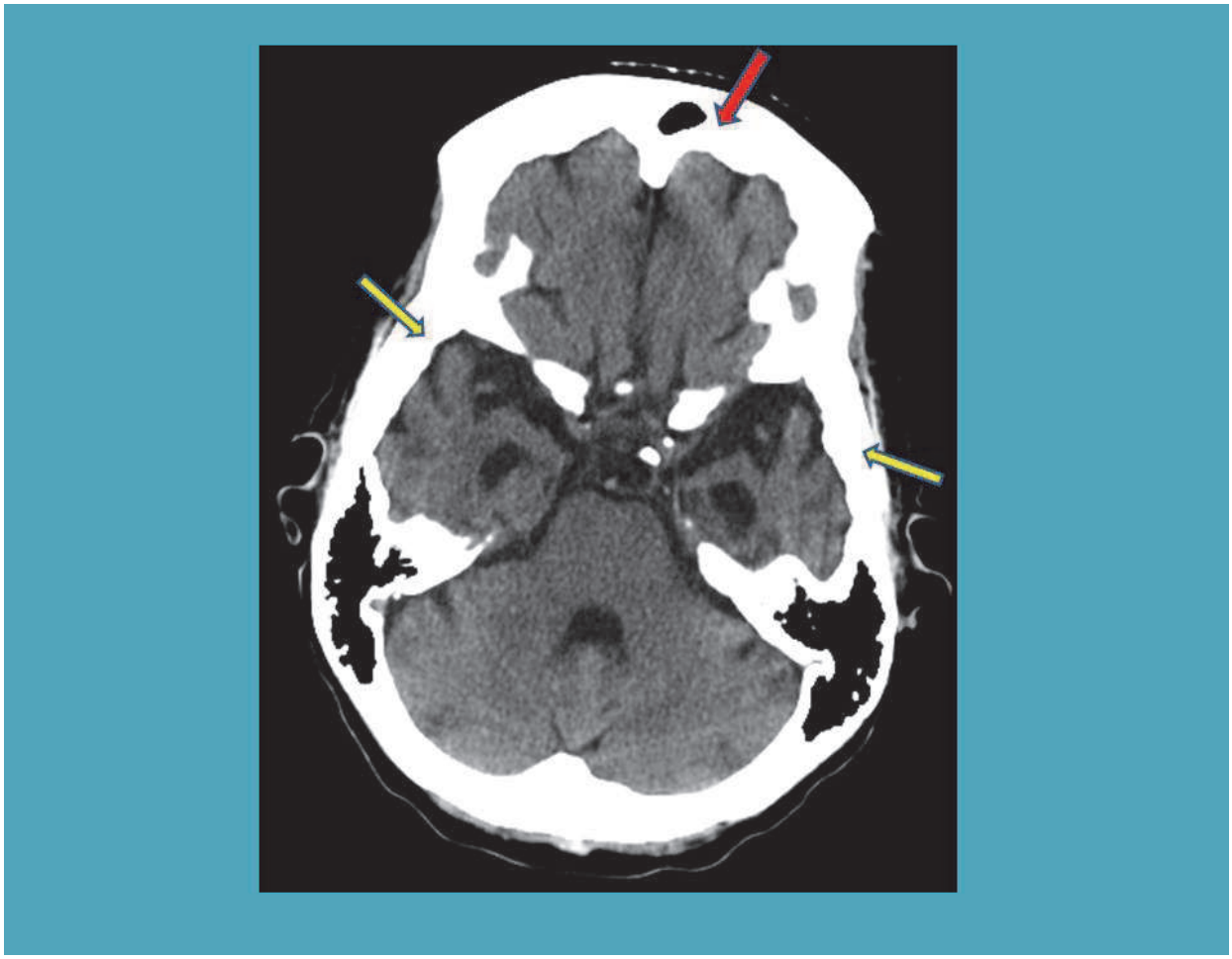
Keywords: Alzheimer disease, DNA consciousness, The interaction-based model of consciousness, Interaction-Complexity-Consciousness (ICC), Selected genetic destination

An Introduction to Alzheimer Disease

A vast amount of research has been accomplished on Alzheimer Disease (AD) over the past 20 years. As a result much has been discovered about the disease pathophysiology and molecular detail of what happens to the neurons and the brain as the disease progresses. In addition, mutations in certain genes have shown a strong correlation in patients who develop AD, which will be discussed later in this article. Prior to discussing the neurogenetics of AD I will give a brief and basic description about AD and what is known about the underlying causes. I will also keep in mind that this is intended for a general audience and I will take the time to explain important terms.

AD is the most common form of dementia that affects more than 37 million people worldwide. Common signs and symptoms of AD are usually memory loss, decline in cognitive functions, and behavioral abnormalities. These signs and symptoms result from prolonged damage to neurons, which results in the loss of brain mass over time. This loss or atrophy of brain mass can be seen on imaging studies such as magnetic resonance imaging (MRI). The MRI on the next page demonstrates gross loss and atrophy of the parietal lobes (seen by the yellow arrows) and also in the frontal lobes (seen by the red arrows) of the brain.

What causes this loss and atrophy of neurons, and ultimately regions of the brain? In the following section I will give a general description of what takes place during the pathological process of AD.



AD MRI: *This is a 77 year old female with progressive AD. Bilateral gross atrophy can be seen in the parietal lobes where the yellow arrows are pointing. Additional gross atrophy is noted in the frontal lobes noted by the red arrow. In general, the gray regions which represent brain mass typically extend further outwards toward the temporal and frontal regions of the skull.*

The disease process of AD starts insidiously in the brain years to decades before symptoms begin to manifest. In fact, according to the new 2011 diagnostic guidelines AD is now understood as a disease that has three phases:

- The asymptomatic preclinical phase- in this phase the disease develops but no symptoms are noticed by the patient, family members, or the medical provider.
- The symptomatic predementia phase- in this phase only mild symptoms appear but they do not seriously impair the patient's everyday life. This is also referred to as *mild cognitive impairment due to AD*.

- The dementia phase- in this phase severe impairments are obvious to the family members, the medical provider, and sometimes the patient. Typically assistance is required for the patient's day to day living in this phase.

These three phases are based on the 2011 AD diagnostic updates which were published in the *Alzheimer's & Dementia* journal and are also reviewed in the 2012 article- *Updated guidelines for the diagnosis of Alzheimer disease: A clinical review*; as well as other publications e.g. the Talan 2011 article and the Budson and Solomon 2012 article. All of these articles are listed in the references and further readings if the reader wishes to explore the updates in more detail.

The pathological process of AD has two main components: the accumulation of a protein call *beta-amyloid* (Aβ) and the formation of *neurofibrillary tangles* (NFT). The formation of NFTs and the accumulation of Aβ begin during the asymptomatic preclinical phase of AD, which is long before the memory impairments, cognitive impairments, or behavioral abnormalities become evident. However, these signs and symptoms do become evident in the symptomatic predementia phase of AD and are more profoundly noted in the dementia phase of AD, which is a result of the progressive accumulation of Aβ and NFTs. I will now briefly discuss the pathological processes of Aβ accumulation and NFT formation.

Beta-amyloid (Aβ) Accumulation

In postmortem studies in patients with AD it has been well established that Aβ accumulation is found in the brain. Aβ accumulates in clusters or plaques, which are also called *senile plaques*. These plaques have been demonstrated to impair the function of the neurons, which after time can cause atrophy and ultimately the death of neurons. But where does Aβ come from?

Aβ is a normal product from the neuronal cell membrane. This is produced when the nerve conducts an electrical impulse. Aβ is derived from a protein called *amyloid precursor protein* (APP). APP is bound in the cell membrane of the neuron and it is released by two different pathways during neuron activity; only one of these pathways releases Aβ. The basic biology behind these two pathways is:

- The Nonamyloidogenic Pathway- APP is acted on by an enzyme called α-secretase and then a second enzyme called γ-secretase. During this pathway no Aβ is formed as an end product.
- The Amyloidogenic Pathway- APP is acted on by an enzyme called BACE-1 and then a second enzyme γ-secretase. During this pathway Aβ is produced.

Note that in both pathways the first enzyme is different (α-secretase as opposed to BACE-1), but the second enzyme is the same (γ-secretase). Please keep in mind that γ-secretase will be important to our discussion on the neurogenetics of AD later in this article.

In the amyloidogenic pathway Aβ is produced and normally broken down by an enzyme called *neprilysin*. However, during the pathology of AD there is an upset in the balance between the production of Aβ verse the breakdown and clearance of Aβ. This leads to the accumulation of senile plaques. Several mechanisms have been proposed to account for this, but the exact reason is at this point in time elusive and debatable. In fact, there are perhaps multiple reasons why this accumulation takes place in the brain.

Neurofibrillary tangle (NFT) formation

The second abnormal pathological feature that occurs in AD is the formation of NFTs. Again, I will keep the description basic and brief, but a general understanding is important.

The outside of the axon portion of the neuron is coated with self-assembling units called microtubules, which are composed of tubulin. The whole length of the axon is covered with microtubules that function as the main cytoskeletal track for axonal transportation. During axonal transportation proteins and enzymes can attach to the microtubules and move along the axon. For example, mechanochemical enzymes that are attached to the microtubules move products that are referred to as *cargo*. The cargo can be vesicles containing protein products, organelles (e.g. mitochondria), polymers of the cytoskeleton, and neurotransmitters. This axonal transport is vital to the function of the neurons and flows in two directions:

- Antrograde- this flows from the body of the neuron to the tip of the axon.
- Retrograde- this flows from the axon tip towards the neuron cell body.

The microtubules on the axon portion of the neuron are held together by a group of four proteins called microtubule-associated proteins- R1, R2, R3, and R4. The group of four microtubule-associated proteins is bound together by another protein called *tau protein*. During the biological activities of the neuron the tau protein picks up a phosphate ion and becomes *hyperphosphorylated tau*. Normally, this phosphate ion is released and normal tau protein continues to function.

In AD this accumulation of phosphate ions continues and eventually the tau protein becomes so hyperphosphorylated that it detaches from the microtubule-associated proteins and the microtubules on the neuron. This causes destabilization of the microtubules and impairment in the transportation mechanism along the axon of the neuron. Without axonal transportation to replenish the cellular constituents of the neuron, in addition to the loss of microtubule stabilization the neuron begins to fall apart.

After the hyperphosphorylated tau protein detaches from the neuron it tends to form *paired helical filaments* with other hyperphosphorylated tau proteins as they have an affinity to pair up with each other. These paired helical filaments form the NFTs that are found in the brains of patients with AD.

This is a very general account of what takes place during the pathology of AD. I have explained the important aspects which will be important in other sections in this paper. In particular, when I discuss the neurogenetic phases that are associated with DNA consciousness and the gene mutations involved in AD. However, before I discuss these two topics I must first give a brief introduction to the theory of DNA consciousness and the proposal of three neurogenetic phases of consciousness.

An Introduction to the Theory of DNA Consciousness

The theory of DNA consciousness originated in 2005.[1] In 2009, this theory transformed from a simple statement into a more involved synthesis. This theory, in a very basic sense, states two

[1] Technically this was conceived in 2004 but it was not completed until 2005. It was then published as a theory in *The Encyclopedia of Anthropology* simultaneously in two entries; *The DNA Molecule* and *Consciousness*- consult the references for further information.

things: that the DNA molecule has a *degree* of consciousness of its own and that the DNA molecule gives rise to other *higher degrees* of consciousness. Before I go into any more detail regarding DNA consciousness, allow me to explain two other concepts: the interaction-based model of consciousness and interaction-complexity-consciousness (ICC).

Interaction-based Model of Consciousness and Interaction-Complexity-Consciousness

The current definition of the interaction-based model of consciousness states that consciousness is the interaction of things (e.g. an organism, DNA molecule, or atom) with other things, the external environment, and more specifically the interaction of energy with other forms of energy. This model is a fundamental way of viewing consciousness. By striping down to the bare bones and avoiding misleading notions like brain verse mind or spirit verse material, the notion of what consciousness is becomes a bit more lucid- interactions. Without interactions consciousness cannot exist in material or spiritual form (to take both sides of the argument). Without interactions consciousness at any degree would appear frozen.

These interactions, and therefore consciousness, begin on very small and fine scales beginning in the quantum world. In previous works of mine quarks were used as the smallest scale, or the smallest degree of interactions, but string theory proposes that the scale is smaller and finer. At this point string theory has not been proven to be testable at this stage of humankind's technological development, and due to this limitation the line will be drawn at quarks as they have been tested experimentally.

As quarks interact with each other and the quantum environment they combine to form subatomic particles- neutrons, electrons, and protons, which produce atoms. Each atom has physical properties of their own, which is defined by the number of protons in the atomic nucleus. Neutrons cluster with the protons and cause slight variations among the atoms with the same number of protons. These are known as *isotopes*. The electrons orbit the atom and are the particles that interact with other atoms. At this stage the atoms begin to interact together and they form elements and molecules.

There is a proposed degree of consciousness that takes place at the level of quarks and subatomic particles known as *quantum consciousness* and as atoms interact they evolve onto *atomistic consciousness*. However, as the interactions at this level begin to increase we also see an increase in the complexity of matter- from quarks to atoms to molecules. It can also be seen that as the degree of complexity in matter increases the degree of consciousness increases. Therefore, at this point we can see that the interaction-based model of consciousness transforms into a concept called *interaction-complexity-consciousness* (ICC) where the notion of complexity is what links the interactions with degrees of consciousness. In previous works I have described this as a simple linear relationship: interactions (complexity) = degree of consciousness, but I also realize that it is probably far more complicated, but this creates a starting point.

Another way of interpreting this is that the degrees of consciousness are dependent on the complexity of its state of matter, and that complexity is determined by the interactions that are allowed. For example, a water molecule has two hydrogen molecules and an oxygen molecule. This water molecule has degrees of freedom and is able to interact to X number of ways and therefore has Y level of complexity, which gives it a degree of consciousness equal to XY. However, a cell for example, is much larger and complex as it is a conglomeration of millions of proteins, water molecules, and nucleotides. This conglomeration allows a higher number of interactions and thus has a higher level of complexity. Collectively, the cell yields a much larger XY, which in turn gives rise to a higher degree of consciousness as compared to a single water

molecule. Additionally, when cells evolve into neurons, which can work in large specialized groups and give rise to a brain we can now appreciate a significantly larger number of interactions that give rise to an even higher level of complexity that results in a higher (*XY*) degree of consciousness.

In this interpretation of the ICC each collective system is a summation of what some physicists refer to as *charge mass aggregation*. Ensconced in the aggregation is an interaction-based complexity that gives rise to consciousness that ascends in degrees base on that interaction-based complexity.

The ICC was discussed in much more detail in the 2011 article The DNA molecule is autopoietic, dynamic, evolving, and a form of consciousness and in the forthcoming chapter DNA Consciousness: From Theory to Science.2 However, what is important here is DNA consciousness. There is a certain point in the evolution of the organic world where the molecules interact and develop nucleotides. This is the first special thing that happens in the ICC- the emergence of nucleotides. This is significant because the nucleotides become RNA and DNA. There is an entire network of RNA that works to produce proteins, which have biological activities and are the building blocks of cells. RNA also performs biological functions as well. DNA can store genetic information and produce many RNA species. Keep in mind, DNA is not just a genetic warehouse or cook book, it operates in a manner consistent with a degree of consciousness3- DNA consciousness.

Once this point of complexity is established with the emergence of nucleotides an explosion takes place. The nucleotide network consisting of DNA and RNA allows a higher scale of interactions. In addition, the various protein products that are made increase the scale of interactions as well. This collective increase in interactions in turn increases the degrees of complexity e.g. the construction of cells, which then increases the degree of consciousness seen in the emergence of cells known as- cellular consciousness.

In the 2011 article The DNA molecule is autopoietic, dynamic, evolving, and a form of consciousness I discuss some of the genes that allow the evolution of prokaryotes to eukaryotes, which again fuels another increase in the degrees of complexity and subsequently consciousness. In that work I also discussed cellular consciousness and the theories of thinkers in the field pertaining to the degree of cellular consciousness. I will not go into detail here as the reader can refer to the references.

From the degree of cellular consciousness the ICC continues in an ascending trajectory from cells to multicellular organisms and eventually to animals with brains and more complicated neural networks. Again, this is discussed in more detail in other works. However, the take home point is this- the interaction-based model of consciousness transforms into the concept of the ICC. Within the ascending trajectory of the ICC the degree of DNA consciousness emerges and then DNA consciousness allows higher degrees of consciousness to emerge- cellular consciousness and eventually human consciousness.

---

[2] This chapter will be published in Ingrid Fredriksson's *Aspects of Consciousness II* McFarland Publications (forthcoming).

[3] What is meant by this is that the DNA molecule does not perform any of its functions at random. There is an autopoietic form of intention, which denotes a degree of consciousness. This is seen in genetic systems were genes control other genes in a network of activation and deactivation.

Back to DNA Consciousness

Now that I have explained the interaction-based model of consciousness and the ICC adequately I will now refocus on the theory of DNA consciousness. DNA consciousness is a degree of consciousness that emerges with in the ICC. This degree of consciousness is the amalgamation of the interactions of DNA, RNA, and the protein products directly involved in the genomic and epigenetic network- this would also include products e.g. transcription factors and polymerases. This collection of interactions seen at the degree of DNA consciousness gives it three dynamic levels that can be observed objectively. The three dynamic levels of DNA consciousness are:

- **Level one-** the interactions between DNA and itself. These interactions include genomic inheritance and DNA replication. There are also thousands of gene-gene interactions that begin as early as fertilization and continue throughout the lifespan of the organism.
- **Level two-** the interactions of DNA and other nucleic entities e.g. RNA, viruses, the mitochondria, and other cells (cell-cell interactions). The interaction between the genome of the host DNA and the DNA (or RNA) of other cellular organelles is known as genomic symbiotics or genetic symbiosis.
- **Level three-** the interaction between DNA and the external environment beyond the cell or body of the organism. DNA is capable of doing this because it is an autopoietic system which by definition one of the requirements are that it is *mechanistic* i.e. subject to cause and effect. The third dynamic level of DNA consciousness is significant in that it illustrates that the DNA molecule is not a closed system and can be affected by interactions with the environment e.g. radiation and mutagens that can cause cancer.

Please keep in mind this is a basic outline and a more detailed survey is completed in the forthcoming chapter *DNA Consciousness: From Theory to Science*.

In summary of this section, DNA possesses that ability to self-assemble and to then store vast amounts of genetic information. This gives DNA the ability to give rise to larger scales of complexity in an extremely reliable fashion- which enforces the notion of intentionality as opposed to a completely random process. When DNA gives rise to the emergence of higher degrees of consciousness it is accomplished by the control of master genes that activate and deactivate other genes throughout the process. This process continues throughout the lifespan. In the case of human consciousness this is divided into what I call *the three neurogenetic phases of human consciousness*, which I will discuss next.

The Three Neurogenetic Phases of Human Consciousness

I have already explained that once the degree of DNA consciousness emerges in the ICC it begins to give rise to higher degrees of consciousness, which ascends up to the level of human consciousness. This is not to imply that humankind is a teleological endpoint! Here I have broken down the relationship between DNA consciousness and human consciousness into three neurogenetic phases. These three phases are:

- Phase one: the emergence of neuron-based consciousness
- Phase two: the continuum of neuron-based consciousness
- Phase three: the neurodegeneration of neuron-based consciousness

I will now explain these three phases in more detail. However, I will keep the genetic detail very simple when I discuss the gene families and leave the reader to consult the references for further information.

Phase One: The Emergence of Neuron-based Consciousness

In this phase there are entire families of genes that give rise to brain regions and sensory organs, which will ultimately provide the machinery for human consciousness. Here are a few of the important ones that have been studied:

- Hox gene family- This family of genes is responsible for the pattern of body segmentation. Some Hox genes are also responsible for the correct development of specific brain regions and act as neural enhancers.
- The Otx1 gene and Otx2 gene- These two genes are considered a subgroup of the Hox gene family. They have been shown to be important in the development and maturation of important brain regions. Otx 1 has been demonstrated to be important to the development of the neocortical area, the hippocampus, the mesencephalon, and the cerebellum. Otx 2 has been demonstrated to be critical in forebrain and midbrain formation.
- Pax gene family- This family of genes has been shown to be involved in the development of some brain regions and sensory organs, in particular the eyes and ears. Some Pax genes have also been shown to control the activity of certain Hox genes.

In addition to the genes that are mentioned here there are many more especially genes that code for neurotrophic factors that are vital to the development of neurons prior to the organization of the brain and central nervous system. For now we will keep it simple and pertinent to our discussion.

Phase Two: The Continuum of Neuron-based Consciousness

This phase takes place throughout the lifespan and is where the genome maintains the function of the neurons and more importantly the ability of neurons to change and make new connections to other neurons. The ability of the neurons to change and form a new connection to other neurons is called *neuron plasticity*. This dynamic process gives the brain the ability to change and is extremely important to human consciousness. There are many genes that are known to be involved in neuron plasticity I will explain a few of them here:

- Brain-derived neurotrophic factor (BDNF) gene- This gene produces BDNF which is involved in memory and associative learning processes. These processes utilize neuron plasticity and BDNF is critical for this to take place. The BDNF gene also is involved in the early formation of the hippocampus and other associated brain regions therefore it can be associated with more than one neurogenetic phase of human consciousness.
- FosB-delta gene- This is a gene from a family of genes known to be involved in neuron plasticity. Many studies have demonstrated that drugs of abuse, including opioids and alcohol, have an affect on these genes which result in loss of brain mass in regions e.g. the amygdala and associated white matter tracts. This can lead to alterations in emotional states and the perception of pain.

- Fibroblast-growth factor-2 (FGF-2) - Similar to BDNF gene, this gene has been demonstrated to be involved in memory. Some studies have demonstrated that FGF-2 activity is lower in individuals with depression and also in AD. Later in this article I will discuss novel gene therapies involving the FGF-2 gene that may one day cure AD.

In addition to these genes that are involved in neuron plasticity, which have a profound effect on the continuum of human consciousness, there are also several genes that are strongly associated with neuropsychiatric disturbances. In other articles and presentations I have discussed PTCHD1 locus disruptions linked to autism, PDE4B gene deletions associated with schizophrenia, Slitrks gene family genetic abnormalities that are involved in obsessive compulsive disorder and schizophrenia, mutations in the EMX2 gene involvement in mental retardation, mutations in the PAK3 gene that results in X-linked mental retardation, and mitochondrial cytopathies that affect degrees of human consciousness.

I will not go into detail here but it is important to know that the second neurogenetic phase of human consciousness covers a much wider area and involves many genes, and many more to be discovered in the future. However, at this point I will continue on to the third neurogenetic phase and then address genes involved in AD.

Phase Three: The Neurodegeneration of Neuron-based Consciousness

During this phase the brain undergoes atrophy and the process of degeneration is more noticeable. This process takes place normally in an age-dependent fashion but is much more accelerated in diseases like AD. Evidence of the loss of brain can be seen on the MRI mentioned earlier in this article. As this disease progresses the person's modalities of consciousness decrease in effectiveness e.g. ability to remember people, places, or where they are. I mentioned earlier in this article that there are genes that demonstrate a strong correlation to AD. These are also known as AD genes. I will now discuss the neurogenetics of AD in order to illustrate an example of the third neurogenetic phase of human consciousness.

The Amyloid Precursor Protein gene

I had mentioned amyloid precursor protein (APP) earlier in the article when discussing the production of Aβ during the pathogenesis of AD. APP gene produces APP, which is an integral membrane protein that is in the cell membrane of the neuron. It functions to regulate synapse formation, neural plasticity, and iron export. The enzyme γ-secretase performs proteolysis on APP and generates many forms of Aβ in the amyloidogenic pathway discussed earlier in this article. Mutations in the APP gene have been strongly associated with the occurrence of AD.

PSEN1 and PSEN2 Genes

These two genes produce the proteins Presenilin-1 and Presenilin-2, respectively. Both of these proteins help to form the γ-secretase complex, along with two other proteins- nicastrin and APH-1. The γ-secretase enzymatic complex performs proteolytic cleavage on the APP- this was mentioned earlier in our discussion on Aβ accumulation. Mutations in these two genes have been strongly associated with the occurrence of AD. It is proposed that mutations in the PSEN1 and/or PSEN2 genes produce abnormal protein variants of PSEN1 and PSEN2 proteins.

Consequently, an abnormal version of the γ-secretase complex is formed and may contribute to improper proteolysis of APP resulting in the abnormal accumulation of Aβ.

The APOE-ε4 Gene Variant

The APOE-ε4 gene produces the apolipoprotein-ε4 (APOE-ε4) protein. This was the first AD risk gene identified. The APOE-ε4 protein can influence brain structure by affecting synaptic generation, other restorative mechanisms involving cholesterol transport, and metabolism in the neurons.

Carriers of the APOE-ε4 allele variant show an increased risk for developing the late-onset disease from of AD. This is known to happen in a gene dose-dependent manner. For example, it has been shown that individuals with one APOE-ε4 allele variant have a three to four-fold increase in the risk of developing AD. However, if an individual inherits two APOE-ε4 allele variants there is a ten-fold increase in the occurrence of AD

I have mentioned four AD genes that have been extensively investigated. However, we must keep in mind that others are under investigation. So in the near future we may have many more genes to discuss that cause neurodegeneration in the brain, which results in the decrease in the continuum of human consciousness.

Connecting DNA Consciousness to the Neurogenetics of Human Consciousness

I have discussed three neurogenetic phases that account for human consciousness. In each of these phases I have illustrated some genes that are known to be involved. But how is DNA consciousness involved? I will attempt to answer this question in regards to each of the three phases.

During neurogenesis a genetic cascade is initiated that eventually constructs the human brain and central nervous system. This is not a random occurrence. There is orchestration conducted by a degree of consciousness i.e. DNA consciousness which regulates this process. If there are mutations or deletions to any of the genes that I mentioned (or others that are not mentioned) in the first neurogenetic phase the ensuing effect is that the brain does not develop properly. This affects the interactions that the brain is able to execute and as a result the complexity is reduced and so is the degree of consciousness.

During the continuum of neuron-based consciousness the neurons rely on protein products to function properly. These proteins are produced by certain families of genes. The neurons also depend on the ability to change and make new connections to other neurons as new information is encountered. In this way neuron plasticity is vital to the continuum of human consciousness. These processes are not randomly running by chance. They are under the control of the degree of DNA consciousness. If genes vital to neuron plasticity are adversely affected or gene abnormalities that cause neuropsychiatric disturbances occur the result is that the degree of DNA consciousness is decreased and the continuum of neuron-based consciousness if affected. In either of these situations the neurons now interact at a lower level, which results in a decrease in complexity and consequently in a decrease in the degree of neuron-based consciousness.

During neurodegeneration there is loss of neurons and loss of brain mass. I have demonstrated that mutations in certain genes can cause downstream effects that contribute to the development of AD. In this process there is an accelerated loss of neurons and brain mass. We now know that gene mutations are involved in this process. This demonstrates that genes, in this

case abnormal ones, can cause decreases in modalities of consciousness and cognition. Looking at it the other way is that when these genes function normally they contribute positively to the continuum of human consciousness. Therefore, there is a neurogenetic connection in both directions as far as the continuum and breakdown of human consciousness is concerned. However, it is the degree of DNA consciousness that has a dynamic effect on the brain's ability to interact. When the interactions of the neurons are decreased then the complexity and ultimately the degree of neuron-based consciousness are both decreased in a descending fashion.

The three neurogenetic phases of human consciousness demonstrate a direct connection between DNA consciousness and neuron-based consciousness. Microscopic effects at the level of the nucleotides can be manifested on the macroscale level of the brain. At this point I have demonstrated several examples in all three neurogenetic phases. As more research is completed the proof of this relationship will become more obvious.

In the future humankind will be able to develop genetic therapies to fix some of these neurogenetic abnormalities that affect human consciousness in all three neurogenetic phases. However, the development of genetic therapies to correct diseases like AD may also be used to enhance modalities of human consciousness in individuals who are not afflicted with the disease. Before I go into this it is important to explain the concept of SGD.

Selected Genetic Destination (SGD)

SGD is the process of altering any organism's genome with genetic engineering technology. In this process a *genetic destination* of a genome is *selected* and made possible with genetic manipulation of the original genome. I included a brief section on DNA consciousness at the end of my chapter on *DNA and Genetic Engineering* which was published in the two-volume reference handbook ***21st Century Anthropology***. In this work while discussing DNA consciousness I proposed that in the future genetic engineering may enable scientists to further explore how DNA is able to interact with itself, with other molecules and cells, and with the external environment. These are the three dynamic levels of DNA consciousness that were already discussed in the previous section on DNA consciousness. Furthermore, genetic engineering may enable humankind to enhance its very own degree of neuron-based consciousness. I will discuss one possibility in the next section of this article.

In a subsequent 2010 publication in the ***International Journal of Arts and Sciences***-*Selected Genetic Destination: The Rise of Homo Sapiens Genomicus* a more detailed account of SGD was given. I will address two important implications of SGD that are significant to DNA consciousness that were addressed in that article.

The first was that with the advent of genetic engineering significant improvements could be made in humankind's degree of neuron-based consciousness. This could be accomplished by creating *aggressive human enhancements*[4] that would improve specific elements crucial to neuron-based consciousness. For example:

[4] In the article *Selected Genetic Destination: The Rise of Homo sapiens genomicus* I made the distinction between *passive human enhancements* and *aggressive human enhancements*. The general definition is that passive human enhancements are genetic therapies to correct an underlying medical defect. On the other hand aggressive human enhancements are genetic therapies aimed at enhancing certain attributes i.e. height or memory beyond what I termed *the subjective median* of [genetic] functioning. This distinction was in order to defend the notion

- increased memory
- the ability to perceive more regions of the electromagnetic spectrum
- increased neuron density that would improve brain capacity
- increased neuron-neuron interconnections
- enhance neuroplasticity

These types of aggressive human enhancements could give rise to a new subspecies *Homo sapiens genomicus* or ultimately, new species with a higher and superior degrees of neuron-based consciousness.

The second important theme discussed in the 2010 IJAS article was the hypothesis that the degree of DNA consciousness has a *will* of its own. If DNA consciousness is the driving force behind all biological evolution and responsible for the emergence of neuron-based consciousness then perhaps humankind was only meant to be transient. That is to say that DNA consciousness, through natural selection, gave rise to the emergence of *Homo sapiens sapiens* and the ensuing higher degree of neuron-based consciousness for the sole purpose of discovering the DNA molecule and unlocking its secrets. The implication being that the DNA molecule discovered itself through the vessel of humankind. This knowledge of DNA and how to manipulate it will eventually provide a new means of evolving DNA consciousness i.e. SGD to replace the much slower process of natural selection.

During our discussion of the ICC I mentioned that the assembly of nucleotides was the first special thing to occur. Allow me to briefly review all four special things that take place with the emergence of DNA consciousness in the ICC. This is important to our discussion as SGD is proposed to be the fourth special thing. Thus I would like to briefly fill in the complete list. These four special things are:

- Nucleotides emerge from molecular degrees of consciousness and cause an explosion in complexity and degrees of consciousness by allowing exponentially larger amounts of interactions and the storage of genetic information.
- Eukaryotic cells develop the ability to conduct electrochemical signals over long distances, giving rise to early degrees of neuron-based consciousness. This is possible when cells developed genes that distinguish themselves as neurons. For example, synapsins genes and myelin gene transcriptional regulator are just a few of the genes that allow neurons to become neurons.
- The development of Hox and Pax gene families allow the emergence of vertebrates with cephalization and a centralized nervous system. Antecedent to these genes there were ancestral versions or *orthologs* that existed in the invertebrates. These gene families were mentioned in previous sections of this article.
- SGD- the ability to select a genetic destination and make it happen utilizing genetic engineering. By refining this technology humankind's current degree of consciousness can be enhanced and new degrees can emerge as well.

It is very important to note that all four of these special things that take place in the ICC involve DNA consciousness. The fact that all four of these special things can be studied scientifically should make a compelling case to substantiate the science of DNA consciousness.

---

that any gene therapy is a form of enhancement established on what I called the genetic baseline. For more information please consult this article.

I had already mentioned that implementing SGD would give rise to a new transgenic subspecies *Homo sapiens genomicus*. However, I also pointed out that *Homo sapiens genomicus* was not an end but rather a new point in evolution that could lead to more future subspecies and species. Therefore, it is important to realize DNA consciousness can manifest itself and continue to evolve through SGD. This would be proven if genetic therapies emerged in the future that can improve modalities of human consciousness or the attainment of abilities beyond that of the *subjective medium of functioning* of the subspecies of *Homo sapiens sapiens*.

Are there current examples of SGD that may be able to increase the degree of human consciousness? Yes there are and this brings me to the next topic on a breakthrough gene therapy that is being investigated to potentially cure AD.

Fibroblast Growth Factor-2 Gene Therapy for Alzheimer Disease

In the near future, scientists will some day be able to enhance human consciousness with SGD. An example of this is the research currently being conducted on gene therapy involving fibroblast growth factor 2 (FGF-2) to potentially reverse the memory decline in AD. In 2011, a significant article was published- *FGF2 gene transfer restores hippocampal functions in mouse models of Alzheimer's disease and has therapeutic implications for neurocognitive disorders*. The results of this gene therapy demonstrated a reversal of memory loss in mice with AD. I will not discuss the research methods but this article is listed in the references if the reader is interested in investigating this.

At this point the FGF-2 gene therapy has only been used in transgenic mice with AD. However, even at that degree of consciousness (the mouse's degree of neuron-based consciousness) we can see a reversal of signs and symptoms of neurodegeneration utilizing SGD. Therefore, a gene (in this case FGF-2) that is underactive in the brain contributes to AD, but when genetic therapy adds more of the active gene to that region of the brain there is improvement in AD symptoms and an increase in neuron-based consciousness. This serves as an example of SGD. This also perfectly displays the relationship of the degree of DNA consciousness to the degree of neuron-based consciousness.

Possible Human Enhancement in the Future

I have discussed the FGF-2 gene therapy and the potential that this has to cure AD. However, there is a possibility that this may be used to enhance human consciousness in the future. First and foremost, using gene therapy to correct AD and reverse memory dysfunction is already a form of passive human enhancement. So what would stop research from being done on the same therapy but on people who do not have AD to see if memory is enhanced beyond normal human standards? This is an intriguing question that will ultimately have ethical conflicts as will any aggressive human enhancements. As more and more gene therapies are being researched to potentially treat genetic disorders the potential for these therapies to be used for human enhancements will become more and more real.

Conclusion

I have attempted to effectuate a new dynamic way of viewing and understanding consciousness. This was accomplished by recognizing consciousness as interactions and that these conglomerations of interactions increase complexity, which results in higher degrees of consciousness. The ICC allows consciousness to be defined a massive collection of all things interacting in a dynamic fashion and on different layers of complexity, which give emergence to degrees of consciousness.

At a particular point in the ICC nucleotides assemble and DNA consciousness emerges. After the arrival of DNA consciousness there is now a mechanism in place that is capable of giving rise to higher degrees of consciousness that can emerge in the macroscopic world. As time goes on DNA gives rise to more complex life forms and higher degrees of consciousness. Eventually neurons and brains evolve allowing interactions on a higher scale of complexity.

Once the primate brain evolves and human consciousness appears the world begins to change. Industry and technology explode. In the early 1950's humankind begins to unlock the secrets of the structure of what makes up all life on this planet- DNA. In 1990 the human genome was initiated and in 2003 it was completed. Humankind is now at the point of development where genes have been identified that are responsible for neurogenesis, corticogenesis, hippocampal formation, psychiatric disorders, and diseases that promote neurodegeneration e.g. AD.

A great deal of research is being done on AD. The neurogenetics of the underlying pathology and possible keys for cures are being investigated rigorously. The FGF-2 gene therapy holds promise for a cure and other gene therapies will undoubtedly emerge. The hope is that eventually these gene therapies will be successful in humans.

When humankind crosses the threshold and finally begins to perfect the technology that enables the reversal of disease processes with gene therapies there is only a fine line to cross to creating human enhancements for those who are not ill. SGD may seem as a Sci-Fi pseudoscience, but reckoning is close at hand. When this materializes the only difference between passive and aggressive human enhancements will be the standard median of functioning because the genetic baseline is adjusted in both cases. For example, if gene therapy is used to cure AD and the patient's memory is brought back to the standard median of functioning this is still an enhancement of the genetic baseline. Of course this is a passive human enhancement, but an enhancement none the less. However, would it not be acceptable to genetically enhance an elderly person's memory even if they did not have AD? Normal aging is not a disease, but if the person was losing their memory and it was severely affecting their daily living it might be feasible to treat them with FGF-2 gene therapy. If so then where is the line drawn? This could rapidly open the door to aggressive human enhancements in where individuals with normal memory would seek treatment to exceed the normal genetic standard of functioning.

I have focused on DNA consciousness and used AD as a model disease that affects modalities of consciousness. AD gene therapy also served as a good example to support my proposal of SGD. However, there is a bigger picture here. This is a new age unfurling here. An age in where DNA will no longer need to depend on the tortoise-like pace of natural selection. This will be replaced by SGD.

As of now, we are living in what is considered the post-genomic era. This is the era after the completion of the human genome project in 2003. Humankind is now approaching the age of SGD and soon to see the appearance of the first *Homo sapiens genomicus*. In this age DNA

consciousness can accelerate its growth spurts and give rise to novel species, perhaps species that are more planet conscious or species that do not circumvent morals and ethics for personal gain and the accumulation of wealth.

In closing, humankind need not tremble when the footsteps of the age of SGD become audible. Humankind may instead welcome this age as a friend or partner because essentially humankind evolved for just that purpose i.e. the evolution of higher degrees of consciousness! Now humankind, like DNA, possesses the ability to give rise to higher degrees of consciousness. Only it will be with more direction, precision, and speed.

References and Further Readings

1. Albert, Marilyn et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Associated workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia* 2011; 7: 270-279.
2. Borroto-Escuela, D.O. et al. Fibroblast Growth Factor Receptor 1-5-Hydroxytryptamine 1A Heteroroeceptor Complexes and Their Enhancement of Hippocampal Plasticity. *Biol Psychiatry 2012; 71: 84-91.*
3. Binder, D.K., and Helen Scharfman. Brain-derived Neurotrophic Factor. *Growth Factors 2004; 22(3): 123-131.*
4. Budson, Andrew E., and Paul R. Solomon. New Diagnostic Criteria for Alzheimer's Disease and Mild Cognitive Impairment for the Practical Neurologist. *Pract. Neurol. 2012; 12(2): 88-96.*
5. Bouchard, Maxime et al. Pax2 and Pax8 cooperate in mouse inner ear morphogenesis and innervations. *BMC Developmental Biology 2010; 10:89.*
6. Cowansage KK et al. Brain-derived neurotrophic factors: a dynamic gatekeeper of neural plasticity. *Curr Mol Pharmacol 2010; 3(1): 12-29.*
7. Emery, Ben et al. Myelin Gene Regulatory Factor is a Critical Transcriptional Regulator Required for CNS Myelination. *Cell 2009; 138: 172-185*.
8. Fornasiero, E.F. et al. The role of synapsins in neuronal development. *Cell Mol Life Sci May 2010; 67(9): 1383-96.*
9. Gatz M, Reynolds CA, and Fratiglionin L. Role of genes and environments for explaining Alzheimer disease. *Arch Gen Psychiatry 2006; 63(2): 168-174.*
10. Gaughran, F, et al. Hipposcampal FGF-2 and FGFR1 mRNA expression in major depression, schizophrenia and bipolar disorder. *Brain Research Bulletin 2006; 70 (3): 221-227.*
11. Grandy, John (forthcoming). DNA Consciousness: From Theory to Science. In Ingrid Fredricksson's: *Aspects of Consciousness II*. McFarland Publications.
12. Grandy, John. Updated guidelines for the diagnosis of Alzheimer disease: A clinical review. CME article. *Journal of the American Academy of Physician Assistants 2012; 25(4): 50-55.*
13. Grandy John. What's new in Alzheimer Disease: Biomarkers and Gene Mutations as Aids for Detecting AD Early. *JAAPA 2011; 24(6): 56-57*.
14. Grandy, John. The DNA molecule is autopoietic, dynamic, evolving, and a form of consciousness. *The International Journal of Arts and Sciences 2011; 4(20): 7-28*.
15. Grandy, John. DNA and Genetic Engineering. *21st Century Anthropology 2010: pp. 76-90.* Sage Publications, Inc. Thousand Oaks, California.
16. Grandy, John. Selected Genetic Destination and the Rise of *Homo Sapiens Genomicus. The International Journal of Arts and Sciences 2010; 3(9): 166-190.*
17. Grandy, John. Consciousness. *Encyclopedia of Anthropology. 2006: vol. 2 (pp.563-566).* Sage Publications, Inc. Thousand Oaks, California.

18. Grandy, John. DNA Molecule. *Encyclopedia of Anthropology. 2006: vol. 2 (pp.753-756).* Sage Publications, Inc. Thousand Oaks, California.
19. Henry W. Querfurth, M.D., Ph.D., and Frank M. LaFerla, Ph.D. Mechanisms of disease: Alzheimer's Disease. *N Engl J Med 2010; 362:329-344.*
20. Huang EJ, Reichardt LF. Neurotrophins: roles in neuronal development and function. *Annu Rev Neurosci 2001; 24: 677-736.*
21. Hyman, B.T., Trojanowski J.Q. Consensus recommendations for the postmortem diagnosis of Alzheimer disease from the National Institute on Aging and the Reagan Institute Working Group on diagnostic criteria for the neuropathological assessment of Alzheimer disease. *J. Neuropathol Exp Neurol 1997; 56: 1095-7.*
22. Jack, C.R. Jr. et al. Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia 2011; 7: 257-262.*
23. Kaplan, Gary B. et al. Opiate Sensitization Induces FosB/delta-FosB Expression in Prefrontal Cortical, Striatal, and Amygdala Brain Regions. *PLos ONE 2011; vol 6 issue 8: e23574.*
24. Khachaturian, Z. Revised criteria for diagnosis of Alzheimer's disease: National Institute on Aging-Alzheimer's Association diagnostic guidelines of Alzheimer's disease. *Alzheimer's & Dementia 2011; 7: 253-256.*
25. Kiyota, Tomomi, et al. FGF2 gene transfer restores hippocampal functions in mouse models of Alzheimer's disease and has therapeutic implications for neurocognitive disorders. *PNAS 2011; 108 (49): E1339-1348.*
26. Larsen, K. et al. Expression of the Homeobox Genes *OTX2* and *OTX1* in the Early Developing Human Brain. *J. Histochem & Cytochem 2010; 58(7): 669-678.*
27. McKhann G.M. et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia 2011; 7: 263-269.*
28. Mckhann G.M., Drachman D., Folstein M., Katzman R., Price D., and Stadian E.M. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology 1984: Jul;34(7): 939-944.*
29. Morrison et al. HOXd4 and regulation of the group 4 paralog genes. *Development 1997; 124: 3135-3146.*
30. Mudo G. et al. The FGF-2/FGFRs neurotrophic system promotes neurogenesis in the adult brain. *J Neural Transm 2009; 116(8): 995-1005.*
31. Nolte, Christof et al. Stereospecificity and PAX6 function directs *Hox4* neural enhancer activity along the antero-posterior axis. Dev Bio 2006; 299: 582-593.
32. Querfurth, HW, and Frank LaFerla. Alzheimer's Disease. *N Engl J Med 2010; 362 (4): 329-344.*
33. Sperling, Reisa A. et al. Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia* 2011; 7: 280-292.
34. Talan J. New Guidelines for Diagnosing Alzheimer Disease: First Update Since 1984. *Neurology Today. 2011: Vol. 11 Issue 9.*
35. Yan, Qin et al. Sumoylation activates the transcriptional activity of Pax-6, an important transcription factor for eye and brain development. *PNAS 2010; 107 (43): 21034-21039.*
36. Yan, Qin et al. Protein Phosphatase-1 Modulates the Function of Pax-6, a Transcription Factor Controlling Brain and Eye Development. *The Journal of Biological Chemistry 2007; 282 (19): 13954-13965.*
37. Zechel S. et al. Expression and functions of fibroblast growth factor 2 (FGF-2) in hippocampal formation. *Neuroscientist. 2010; 16 (4): 357-73.*