The Neurogenetic Correlates of Consciousness

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The neurogenetic correlates of consciousness (NgCC) is a new field of consciousness studies that focuses on genes that have an effect on or are involved in the continuum of neuron-based consciousness. A framework of consciousness based on the neural correlates of consciousness (NCC) has already been established by Francis Crick and Christof Kock. In this work I propose that there are NgCC underlying the NCC which are both active during the conscious experience. So how are genes involved? There are two significant connections between DNA and neurons that are involved in the conscious experience. First, any brain system can be adversely affected by underlying genetic abnormalities which can be expressed in an individual at birth, in adulthood, or later in life. Second, the DNA molecule does not lay dormant while the neuron runs on autopilot. DNA is active in translating and transcribing RNA and protein products that are utilized during neuron functioning. Without these products being continuously produced by the DNA during a conscious experience the neurons would cease to function correctly and be rendered unable to provide a continuum of human consciousness. Consequently, in addition to NCC, NgCC must be factored in when appreciating a conscious event. In this work I will discuss and explain some NgCC citing several examples.

Keywords: Neurogenetic correlates, Consciousness, DNA consciousness, Interaction-based model of consciousness, Neurogenetic phases of consciousness.

1. Introduction

The notion of consciousness continues to baffle and mystify man. What has always been problematic in consciousness studies, as well as physics, is the concept of the observer. The phenomenon of the observer has also made it clear that a *quantum enigma* exists, which is where physics meets consciousness [1]. Often when we speak of human consciousness we are referring to, at least partially, the functioning of the brain. Consequently, we could also view the quantum enigma as being where physics meets the neuron. However, we must ask how do neurons and ultimately the brain arise and manifest consciousness? This could shed light on how the phenomenon of the quantum enigma arises.

Currently, global networking models that involve many brain regions that are dynamically interacting have been proposed. The materialist and neuro-biological models of consciousness maintain that human consciousness is a manifestation of the brain and the neurons. In 2003, a framework of consciousness that was based on the neural correlates of consciousness (NCC) was proposed by Francis Crick and Christof Koch [2]. In this proposal brain systems are active in tandem with the conscious experience. More recently specific areas of the brain have been the focus of research. Some of these brain regions were discussed and summarized at the *Towards a Science of Consciousness 2012 Conference* [3]. Here is a brief summary of some of the brain regions that appear to be NCC:

- Areas affected by anesthesia e.g. the frontal cortex integration to the posterior parietal cortex.
- Decreases in brain connectivity and cerebral integration seen in PET scans and fMRI studies in patients in vegetative states (unresponsive wakefulness syndrome) and minimally conscious states.
- Frontoparietal connections that provide a global workspace. Two examples of these connections are: 1) lateral prefrontal and parietal cortices that function to provide *external sensory awareness* and 2) precuneal and mesiofrontal midline activity functions to provide an *internal awareness*.
- Critically emergent properties of collective wide-spread connectivity of consciousness found in the thalamo-cortical regions.

With these four examples above we can appreciate specific brain regions that can extend globally in order to interact during the process of human consciousness. Each brain region is composed of specialized neurons that give that brain region its unique character. Therefore, the proper functioning of the neurons is pivotal to the process of human consciousness as well.

However, is it possible that there is something tangible beneath the neuron?

In previous works I have proposed that the DNA molecule is just as important to human consciousness as the neurons and the brain. In an attempt to establish a genetic account of consciousness I have proposed the neurogenetic correlates of consciousness (NgCC). In this work I will identify several NgCC and discuss their importance to consciousness. However, consciousness is interpreted and defined very differently by scholars and scientists. Before I discuss any of the NgCC I will first establish what I mean by consciousness and how these three neurogenetic phases were derived.

2. The Interaction-Based Theory of Consciousness

There are many different theories of consciousness. When I discuss consciousness I implement the *interaction-based theory of consciousness*. This theory defines consciousness as the interaction of *things* (be it an organism, DNA molecule, or atom) with other *things*, the external environment, different forms of energy, and forces. Essentially this theory maintains that consciousness *is* interactions. By accepting this premise everything in the universe has a *degree* of consciousness ranging from quarks to molecules to cells to brains as they all interact in various degrees. Another way of depicting this is to imagine a universe with no interactions. In this depiction would consciousness exist or would consciousness appear frozen?

If we look at the smaller end of the scale, for example molecules, and observe those interactions we will notice that as the interactions increase in any given system there is a resulting increase in complexity. So the smaller molecules interact and become larger molecules which become more complex and can ultimately give rise to cells. At the cellular level there is a larger degree of consciousness than that of the simple molecules. This is based on the cell's ability to interact on a more complex level than the individual molecule. Therefore, as *things* interact they become more complex.

In this model we also observe that as complexity increases so does the degree of consciousness. For example if an individual cell has a degree of consciousness (sometimes referred to as cellular consciousness or polyzoism) and if we compare this degree of consciousness to a brain we will notice an obvious difference between those two degrees of consciousness. The degree of consciousness seen in the brain is higher due to its biological complexity. Another way of saying this is that the complexity of a system is directly related to the complexity of the consciousness experience or that degree of consciousness.

If we go back to the beginning of this idea of the interaction-based model of consciousness we will see this conceptual relationship emerge- things interact (which is consciousness) and become more complex and as complexity increases so does this degree of consciousness. In this simplistic version the concept of interaction-complexity-consciousness (ICC) can be appreciated. In this concept of the ICC there is a perpetuation that goes in an ascending fashion from the level of quarks to molecules and from cells to multicellular organisms. It is possible that this schematic may reflect a charge-mass aggregation that accounts for this scale dependency. Similar concepts have been proposed by Wolfgang Baer [4]. In the Baer proposal there is a force (Fc) that physically balances mass and charge forces. This involves a cognitive process loop in where a description of a phenomenological experience is converted (in a quantum physics sense) into a description of the model of a physical world that we believe- when applied to human consciousness. The description is then converted back and thus completing the cognitive process loop.

So what does the interaction-based model of consciousness and the ICC have to do with DNA or the neurogenetic correlates of consciousness? Next, allow me to describe the theory of DNA consciousness.

3. DNA Consciousness

While observing the trajectory of the ICC that proceeds in an ascending fashion from low complexity (lower degree of consciousness) to higher complexity (higher degree of consciousness) we can appreciate that something special seems to happen in the molecular realm when nucleotides begin to assemble and give rise to RNA and DNA. The evolution of networks of RNA and DNA allows the emergence of higher degrees of consciousness at the microscopic level with cells and then eventually at the macroscopic scale with the evolution of multicellular organisms. At this point we have DNA and RNA at a particular degree of consciousness and at the same time possessing the ability to give rise to higher degrees of consciousness. This phenomenon is known as *DNA consciousness*.

In essence the theory of DNA consciousness maintains two main ideas. First, that DNA has a degree of consciousness within the ICC where everything has a degree of consciousness. Second, that DNA can give rise to higher degrees of consciousness. However, why does DNA receive all the credit? Is not RNA just as important to the assembly of the cell? The reason why DNA is given precedence over RNA is due to the fact that RNA by itself cannot give rise to macroscopic

organisms and the subsequent higher degrees of consciousness. Although some RNA viruses exist in nature no macroscopic RNA-based organisms have been identified to date.

The theory of DNA consciousness forces us to view DNA as not merely a genetic storage unit. DNA is dynamic, autopoietic, and a form of consciousness [5]. In addition, DNA is required for the transformation of macroscopic scales of consciousness and without DNA consciousness higher degrees of consciousness cannot emerge from the molecular degree of consciousness.

The importance of DNA consciousness in the ICC and development of higher degrees of consciousness lay in the ability of the DNA molecule to create and store genetic characteristics. For example the development of novel genes allows cells to become neurons. Another way of stating this is that in order for neurons to emerge new genes are required to evolve. I will briefly discuss two of these gene families to serve as examples of this statement.

One gene family that plays a significant role in the emergence of neurons is the synapsins gene family [6]. Synapsins I, II, and III are not expressed in other cells, only neurons, and these genes allow the synapses of the neuron to change [7]. This ability of the neuron's synapse to change is known as neuron plasticity. A second gene that is important to the development of vertebrate neurons is the *myelin transcription factor gene* which allows the production of myelin [8]. Myelin is important because it allows faster transduction of nerve impulses. However, the myelin transcription factor gene is only found in the vertebrates.

At this point multicellular organisms begin to evolve that utilize neurons to interact with the environment in a more complex fashion. Once again the development of new genes allows the increase in degrees of consciousness which is the connection that DNA consciousness provides. Another example is when the Hox and Pax gene families emerge and will eventually pave the way for the appearance of the primate brain- some of these genes will be discussed in further sections. These two gene families allow for the centralization and cephalization of the central nervous system. The human brain emerges from this schematic and gives rise to human consciousness. I have proposed that this happens in three neurogenetic phases:

- Phase One: The emergence of neuron-based consciousness
- Phase Two: The continuum of neuron-based consciousness
- Phase Three: Neurodegeneration

Now that I have established what I mean by consciousness and how we have arrived at the three neurogenetic phases of human consciousness- first the interaction-based theory of consciousness gives rise to the concept of the ICC, second within the ICC DNA consciousness emerges, and third DNA consciousness will eventually give rise to neurogenetic correlates of human consciousness that are categorized in three phases. As I stated earlier the NgCC are genes that have an effect on or are involved in the process of human consciousness. Next, I will discuss a few genes in each of the three phases. I will not go into great molecular detail but rather only a brief summary as I discuss these genes in more detail in two other forthcoming works [9, 10].

4. The Neurogenetic Correlates of Consciousness: Phase One

In phase one the focus is on the emergence of neuron-based consciousness. The neurons and brain regions that develop will be the machinery that allows the degree of human consciousness to function. In this section I will briefly discuss four genes that are involved in this phase to use as examples while fully recognizing that many more are active during this process- Pax3, Pax6, Otx1, and Oxt2.

The Pax3 gene produces the Pax3 protein which is a transcription factor. This is active during the formation of neural tube. It is also serves a mandatory function in the closure of the neural tube and this is accomplished by p53 ubiquitination which is the inactivation of a protein by attaching the regulatory protein ubiquitin [11]. The p53 protein is signification in the cell cycle as it delays the transition from G1 phase to G0 phase. During neural tube development cells divide undifferentiated in G1. In G0 mitosis suppressor proteins activate tissue specific proteins. Closure of the neural tube needs to be complete prior to this is and Pax3 is vital to this process.

The function of the Pax3 gene is significant to the proper formation of the neural tube in the early embryonic stages of development. However, it also acts as a 'master gene' that controls the action of other genes involved in brain formation. For example it has been demonstrated that Pax3 regulates the Hes1 and Neurog2 genes, which is done by acetylation (the addition of a $COOH_3$ group) [12]. These two genes have very important roles in the development of the brain. Hes1 is involved in the maintenance of neural stem cells that determine what type of neurons will develop in the nervous system and Neurog2 plays a role in the specification of neuronal subtypes, sensory neurogenesis, and neural crest cell neurogenesis.

Another example of how Pax3 acts as a master gene

is demonstrated when it interacts with Pax7 to regulate Meis2 which is required for the development of a region of the brain called the tectum [13]. The tectum is located in the midbrain and is made up of the inferior colliculi and superior colliculi which perform an auditory and visual function, respectively. This is a more specific example of how Pax3 is involve in the control of another gene (Meis2) that gives rise to a region of the brain that is involved in human consciousness.

Pax6 is a highly conserved gene in the animal kingdom and is involved in eye development [14]. It also is involved in the regulation of Spag5 which is associated with spindle machinery and regulation of kinetochore microtubule dynamics during cell division [15], influences the fates of the glial promoter cells of the forebrain [16], and regulates the neurogenesis or Neuro-Glia2 progenitor cells in the hippocampus [17]. Additionally, Pax6 is also involved in the proper development of the thalamocortical neurons [18] which are extremely significant to human consciousness. Recall that critically emergent properties of collective widespread connectivity of consciousness that is located in the thalamocortical regions was one of the NCC mentioned earlier in the introduction.

Two homeobox genes (Hox) Otx1 and Otx2 are required for the formation of a region in the embryonic brain called the zona limitans intrathalamica (ZLI) [19]. The ZLI is an important developmental boundary that is crucial for the development of the thalamus. Otx1 and Otx2 are also important for the development of the midbrain in the anteroposterior direction and dorsoventral direction [20]. This is accomplished by a dose-dependent antagonism of Shh gene in the dorsoventral direction and the Fgf8 gene in the anteroposterior direction.

These two genes have additional roles in the development of other brain regions. The Otx1 gene is critical for the development of the neocortex [21] and also affects the overall size of the cerebral cortex [22]. The Otx2 gene is critical in the development of the diencephalon, mesencephalon, choroid plexus, basal telencephalon, and hippocampal anlage [21] and regulates the neuronal progenitor domains of the ventral midbrain (tegmentum) [20].

What does Pax3, Pax6, Otx1, and Otx2 tell us about the emergence of neuron-based consciousness? The functions that I have enumerated demonstrate that the emergence of human consciousness is an orchestrated event that depends on the interactions of many genes, with some acting as master genes. This is not a random event that serendipitously evolved. It is a degree of consciousness- DNA consciousness which humans cannot perceive but can appreciate the end result.

5. The Neurogenetic Correlates of Consciousness: Phase Two

In phase two the focus is on the continuum of neuron-based consciousness. This continuum is composed of the continuous series of neuronal events active during the continuous seamless process of human consciousness. In phase one we saw that genes acting under a degree of consciousness- DNA consciousness give rise to the parts of the brain that will give rise to human consciousness. After the parts of the brain are formed DNA needs to dynamically and continuously be active in tandem with the conscious experience. In this section I will briefly discuss seven genes (some are transcription factors that are altered versions of the original gene product)- PTCHD1, three schizophrenia-associated genes (PDE_4B, $DISC_1$, and ZNF804a transcription factor), BDNF, FGF2, and the ΔFosB transcription factor. I will demonstrate that when there is a malfunction of some of these genes e.g. a mutation, deletion, or a single nucleotide polymorphism (SNP) that there is an adverse effect on the degree of human consciousness.

Disruptions in the gene locus of the PTCHD1 gene are strongly related to autism-spectrum disorders and intellectual disability [23]. This is significant in understanding how a gene locus disruption can have an effect on the continuum of human consciousness as autism is a well characterized clinically. In autism there is impairments in the abilities to communicate and socialize; particularly with reciprocal interactions. These patients appear introverted and out of touch for the most part with the external world.

Schizophrenia (SZ) is a mental illness in where there is a noticeable disturbance in the sensorium, improper processing of information in the brain, and the perception of stimuli that is not actually there e.g. visual and auditory hallucinations. Other symptoms accompanying SZ can be paranoia and delusions in where the patient misinterprets reality. Recently several SZ-associated genes have been under investigation. Here I will discuss three of them.

Two gene mutations have shown a strong correlation with SZ. The PDE4B and DISC1 genes produce the two proteins respectively that form the PDE4B-DISC1 complex. Mutations in either of these two genes which would result in a dysfunction of this complex have been strongly implicated in many of the molecular mechanisms underlying SZ [24, 25, & 26]. Although PDE4B and DISC1 interact extensively they also have individual functions. PDE4B regulates cAMP signaling cascades in neurons and is involved in the synaptic plasticity during learning and memory. DISC1 serves as a part of the microtubule organizing center called the centrosome, as well as being involved in cytoskeletal processes in neuronal migration.

ZNF804a is a transcription factor that regulates the expression of PDE4B and three other genes- PRSS16, COMT, and DRD2, which are all considered SZ-associated genes. So once again we have an example of a gene that regulates other genes that can have an effect on the continuum of consciousness. Recently ZNF804a expression has been proposed as a candidate mechanism that confirms SZ risk [27]. This is due to the fact that it influences the expression of these other SZ-associated genes.

Neuron plasticity is the ability of neurons in the brain to change and make new connections with other neurons or dissolve weakened connections. This happens every day and gives the brain the ability to change in response to new information. Neuron plasticity has been associated with the BDNF gene, FGF2 gene, and ΔFosB transcription factor.

BDNF and FGF2 genes produce proteins that are well known neurotrophic factors that play vital roles in neuron plasticity which underlies processes e.g. learning and memory [28, 29]. Both genes are also known to have decreased activity in disorders e.g. major depressive disorder and Alzheimer's disease [30, 31]. However, I will not discuss these genes in detail as I have done this in other works [9, 10]. At this juncture it is important to note that these two genes are associated with neuron plasticity and when either of their activities are decreased there is an association with decreases in degrees of consciousness that are observable in disorders like Alzheimer's disease and major depressive disorder.

The ΔFosB transcription factor, which is a truncated product of the FosB gene, is involved in neuron plasticity in regions of the brain e.g. the amygdala. The amygdala is involved in many processes that are important to consciousness i.e. in pain perception and rating the emotional response to the environment. The expression of the ΔFosB transcription factor can be affected by opioids which can result in the decrease volume of the amygdala seen on brain imaging studies [32]. These changes in the amygdala also have demonstrated correlations to clinical symptoms associated with addiction e.g. opioid-induced hyperalgesia (an increase in pain sensitivity secondary to opioid use) and hyperkatifeia (a hypersensitivity to negative emotional states and/or increased intensity of emotional distress secondary to opioid use) [33]. The ΔFosB transcription factor has been shown to affect the expression of several genes; for example it induces the expression of GluR2, Cdk5, and NFκB genes, whereas it represses the expression of the dynorphin gene [34]. Addiction is also interesting in relation to consciousness as addictive behaviors tend to be counter intuitive to self-preservation. These changes in gene expression cause profound changes in the central nervous system which contribute to drug-seeking behavior.

So what do the genes that were discussed in the second phase tell us? They demonstrate that disruptions or mutations in certain genes can have an affect on modalities of human consciousness, which can be manifested as disorders like autism and SZ. Secondly, drugs can affect genes that have downstream affects on brain regions that can influence the continuum of consciousness. Lastly, one gene product can influence several other genes that can affect multiple brain regions. This was seen with the ΔFosB and ZNF804a transcription factors.

Overall there is a collective genetic system that possesses a degree of consciousness which in turn gives rise to the continuum of human consciousness. If there is any damage or abnormal expression in certain genes an observable change in the continuum of human consciousness can be manifested which can be studied objectively.

6. The Neurogenetic Correlates of Consciousness: Phase Three

In phase three the focus is on neurodegeneration or the breakdown of the neurons and ultimately brain regions. The breakdown of certain brain regions due to pathological conditions which are involved in the cognitive process illustrates the direct relationship of human consciousness to the brain. In some of these pathological conditions genes are involve and a good example of this is seen in Alzheimer's disease (AD). In this section I will briefly discuss four genes- APP, PSEN1, PSEN2, and APOE-ε4 (and their protein products). These four genes are all strongly associated with AD [35]- in fact these genes are being explored to diagnose AD long before symptoms emerge later in life [36].

One of the main pathological features of AD is the accumulation of beta-amyloid protein in the brain, which eventually causes damage to the neurons. Mutations in any of the four AD genes- APP, PSEN1, PSEN2, and APOE-ε4 are associated with AD as these mutations produce abnormalities which contribute to the accumulation of beta-amyloid.

AD is commonly associated with memory loss, decline in cognitive functions, and behavioral abnormalities. These signs and symptoms are a result of prolonged damage to the neurons. The loss of neurons is what is referred to as neurodegeneration. As already mentioned AD-associated genes can accelerate this process. As the process of neurodegeneration progresses, as seen in AD, modalities of consciousness decline and are eventually lost e.g. the ability to form new memories. Recently the clinical criteria for diagnosing AD have been updated and AD is now

recognized as a disease process that begins years to decades prior to the manifestation of signs and symptoms [37].

So what do APP, PSEN1, PSEN2, and APOE-ε4 genes tell us about the third neurogenetic phase of consciousness? These genes demonstrate a direct relationship to the maintenance of cognitive processes involved in human consciousness [38]. When there are abnormalities in any or several of these genes the molecular effects ensue (in the case of AD beta-amyloid accumulation) and cause damage to neurons and ultimately are manifested as a loss of gross brain mass. This damage translates into decreases in the modalities of human consciousness or more specifically in the degree of consciousness.

7. Conclusion

In this article many NgCC have been discussed and categorized into three neurogenetic phases. It is obvious that these three phases demonstrate a link between DNA and human consciousness: 1) during neurogenesis a genetic cascade is initiated that eventually constructs the human brain and central nervous system which will serve as the machinery of consciousness, 2) during the continuum of neuron-based consciousness the neurons rely on protein and RNA products in order to function properly, and these are continuously produced by DNA, and 3) during neurodegeneration there is a loss of neurons and resulting brain mass which can be cause by genetic mutations. This demonstrates that genes do influence degrees of human consciousness. Finally, by observing the many NgCC enumerated into three phases a connection between DNA consciousness and human consciousness can be appreciated.

In the future more NgCC shall be indentified and a more complete picture will be constructed. In addition, quantum physics may assist in understanding the interactions of the DNA-RNA-protein networks that manifest human consciousness.

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