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Neurogenetics and Human Consciousness

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Human consciousness has historically been an enigma tantalizingly engaged by philosophy. However, the topic of human consciousness was confronted by psychology in the later part of the 1800's, most notably by William James [1]. In due course, a framework of consciousness based on the neural correlates of consciousness (NCC) was proposed by Francis Crick and Christof Koch in 2003 [2]. In this framework brain systems are active in tandem with the conscious experience.

Eventually, a more profound and clandestine phenomenon would be proposed to account for the emergence of human consciousness-DNA consciousness, which was proposed in two previous works in 2006 [3,4]. The theory of DNA consciousness proposes that the DNA molecule gives rise to human consciousness and that DNA possesses a degree of consciousness in its own right [5]. Recently, the theory of DNA consciousness has evolved into *three neurogenetic phases of human consciousness* [6]. In this framework neurogenetic correlates of consciousness (NgCC) function on an underlying scale in relationship to any NCC. In this paradigm NgCC are involved in the emergence, the continuum, and the decline of human consciousness (typically caused by neurodegeneration) i.e. the three neurogenetic phases of human consciousness.

Each of the three neurogenetic phases possesses hundreds, and perhaps thousands, of genes (and gene products) that are pivotal to human consciousness. An early conceptualization and organization of some of these genes and their place in the three neurogenetic phases of human consciousness has been proposed [7]. Some of these genes are involved in more than one neurogenetic phase.

The first neurogenetic phase is the emergence of neuron-based consciousness. The processes involved in brain morphogenesis and the emergence of the central nervous system requires the strict regulation by master genes and trans-activation throughout the developmental hierarchy. This allows undifferentiated progenitor cells to flourish into cells with a specific function and ultimately compartmentalize into specific regions of the brain that become the primary machinery of human consciousness. Certain families of genes are absolutely necessary for these brain regions to come forth to fruition. The following genes are examples of NgCC but by no means a complete enumeration.

The Pax3 gene is required early in embryogenesis [8] and is required for neural tube development and closure [9]; which is the early foundations of the human brain and nervous system. The Pax3 is also responsible for the regulation of the expression of Hes1 and Neurog2 which are important to neuronal stem cell maintenance and the neuronal subtypes [10]; as well as the regulation of the expression of Meis2 which is pivotal for the formation of the tectum [11].

The Pax6 gene is a master regulator of eye development and is highly conserved throughout the animal kingdom [12]. One of the ways Pax6 is critical to eye development is by controlling lens formation. This is accomplished by regulating the expression of four other genes L-maf, Sox1, Prox-1, and lens structural protein crystallins α, β, and γ [13]. In addition, Pax6 is involved in the neurogenetic fates of the glial progenitor cell in the forebrain [14], the proper development of thalamocortical connections [15], and the regulation of neurogenesis of neuron-glia2 progenitor cells in the hippocampus [16].

The Hox genes are important determinants of the anteroposterior (AP) patterning of all embryos throughout the animal kingdom [17]. However, several Hox genes also control brain morphogenesis. Otx1 and Otx2 are Hox genes that have been shown to be expressed in the human brain during weeks 7-14 [18], and both genes are required for the full development of the thalamus; particularly the zona limitan intralamica [19]. In addition, Otx1 is critical for the formation of the neocortex and for the overall development of the cerebral cortex [18]; and Otx2 is critical for the formation of the diencephalon and hippocampal anlage [18]. Other examples of Hox genes that are involved in brain morphogenesis are Hoxd4 and Hoxb4, which are neural enhancers that enforce the border of the anterior brain and rhombomeres 6 and 7 in the hind brain [20,21].

Using only six genes as examples, it can be visualized that these NgCC have a profound impact on the emergence and proper functional development of the brain, which will ultimately become the primary machinery involved in experiencing human consciousness in the physical world.

The second neurogenetic phase is the continuum of neuron-based consciousness. Several genetic abnormalities can alter this continuum. This can be illustrated by observing the genetic association of several psychiatric disorders that clinically demonstrate disruptions in thought, perception, volition, and interaction with the external environment.

PTCHD1 locus disruptions have been associated with Autism disorder [22,23]. Autism is a disorder characterized by observable deficits in communication, socialization, and reciprocal interactions.

Schizophrenia is a disorder of thought and volition, which is clinically characterized by profound emotional and cognitive disturbances, and often concomitant with defects in cortical activity and hallucinations. Abnormal expression of schizophrenia-associated genes PDE4B [24] and DISC1 [25] have both demonstrated a strong association to schizophrenia. The transcription factor ZNF804a has also been correlated with schizophrenia. This is likely due to the fact that ZNF804a regulates the expression of several schizophrenia-associated genes e.g. PRSS16, COMT, PDE4B, and DRD2 [26].

The continuum of human consciousness requires that neurons in the brain have the ability to change and form new connections in response to new information and stimuli. Therefore, neuron plasticity is an essential feature of human consciousness. BDNF gene is a potent modulator of synaptic plasticity [27]. BDNF is also involved in the maturation of the prefrontal cortex and the hippocampus, and is involved in memory and learning [28]. Polymorphisms in BDNF have

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been associated with decreased modulation of hippocampal plasticity [29]. The FGF2 gene has also demonstrated involvement in the maintenance of neuron plasticity during adulthood [30]. FGF2 is also involved in the proliferation of hippocampal neuron progenitor cells status post traumatic brain injury [31].

The ΔFosB transcription factor, a truncated splice variant of FosB, can be induced by drugs of abuse. While it is induced it can alter the expression of four other genes- GluR2, Cdk5, NFκB, and Dynorphin, which can cause neuroplastic-related morphological changes in the brain and decreases in the connectivity of some of the white matter tracts [32]. These changes can contribute to the clinical syndromes opioid- induced hyperalgesia and hyperkatifeia [33].

With just these few examples we see that genetic pathways can have a significant impact on the continuum of human consciousness during adulthood and abnormalities in pivotal genes can have observable effects that can be manifested as psychiatric disorders and neurological disorders related to neuron plasticity. These disorders can be objectified clinically.

The third neurogenetic phase is neurodegeneration or the erosion of some of the modalities of neuron-based consciousness. This is exemplified very well in Alzheimer disease in which cognitive skills, behavioral abnormalities, and memory loss are common ailments. In 2011, the guidelines for diagnosing Alzheimer disease where updated and this neurodegenerative disease is now recognized in three phases [34]. During the dementia phase of Alzheimer disease a decrease in the degrees of human consciousness is seen i.e. the patient ceases to be whom they once were.

An overwhelming amount of evidence has implicated several genetic pathways in Alzheimer disease. Four genes in particular- APP, PSEN1, PSEN2, and APOE-ε4 have been correlated with this neurological disorder and there is strong hope that affordable and reliable genetic tests may emerge to screen for susceptibility [35]. Early detection may be important as some patients with APOE-ε4 phenotype have been shown to benefit from the oral administration of melatonin while in the mild cognitive impairment phase of Alzheimer disease [36]. This could be due in part to the fact that melatonin is involved in genetic pathways that counteracts the activity of free radicals and enhances DNA repair by its effect on >100 genes [37].

By studying genes associated with Alzheimer disease NgCC are identified, that when those genes do not function properly (due to mutations), and demonstrate a decline in the global functioning of human consciousness. In previous works I have attempted to use these motifs to make a scientific connection between the phenomenon of Alzheimer disease and DNA consciousness [38].

In conclusion, what I have established at this juncture is a starting point in enumerating several NgCC. Hence much more research needs to be completed in order to make the importance of the genetic pathways in which the NgCC serve to function in the three respective neurogenetic phases of human consciousness. However, as of now a feasible proposal has been put forth; a paradigm which may redefine how we understand human consciousness. This could also change the way in which we view DNA- from a mere genetic storage unit to a dynamic entity with a degree of consciousness that has already been scientifically objectified on three dynamic levels [39].

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