Alzheimer Disease and Human Consciousness: A Neurogenetic Connection.


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Editorial Board Member:
The Journal of Neurological Disorders.
The Journal of Biological and Chemical Research.
The World Journal of Biology and Medical Sciences.
During this presentation I will:

- briefly discuss the definition of human consciousness
- briefly discuss the 3 neurogenetic phases of human consciousness
- briefly discuss genes involved in Alzheimer Disease (AD)
- discuss the neurogenetic connection between AD, human consciousness, and the possibility of human enhancement
Defining Human Consciousness

How do we define human consciousness?
This is an area of intense debate with no unilateral agreement!
Defining Human Consciousness

A general definition

Human consciousness is defined as a collective totality of awareness, bodily (or somatic) sensations, perceptions (sensory input and neurobiological information), emotions, thoughts, and recollections of the self within a moment on the time continuum.

Defining Human Consciousness

Other definitions:

- consciousness emerges quite simply from an understanding of neuronal activity
- consciousness is not a discrete operation of the brain but the outcome of computational activity of the associated areas of the brain
- consciousness is a discrete phenomenon and that the issues of subjectivity, unity, and intentionality must be confronted if we are to understand how our experience is constructed

Neural Correlates of Consciousness

Initiated by Francis Crick and Christopher Koch

NCC are the minimal neuronal mechanisms jointly sufficient for any one specific conscious principle.

Within this framework (or proposal) brain systems are active in tandem with the conscious experience.

According to Kandel- NCC demonstrate that there are qualitative differences between the neural activity associated with conscious and unconscious cognitive process.
Neural Correlates of Consciousness

Examples of NCC:

• Areas of the brain that are affected by anesthesia, e.g., the frontal cortex integration to the posterior parietal cortex.
• Decreases in cerebral integration and connectivity to other areas of the brain. This has been demonstrated in studies using PET scans and fMRI in patients with unresponsive wakefulness syndrome (also known as vegetative state) and in minimally conscious states.

Neural Correlates of Consciousness

Examples of NCC:

- Frontoparietal connections in the brain that provide a global workspace. Two examples of these types of connections are: 1) lateral prefrontal and parietal cortices that function to provide external sensory awareness and 2) precuneal and mesiofrontal midline activity, which functions to provide an internal awareness.
- Thalamo-cortical regions that have been shown to provide critically emergent properties of collective widespread connectivity of consciousness.

A Neurogenetic Account of Human Consciousness

The focus on neurogenetics forces us to look beyond the brain and neuron.

There is an entire neurogenetic substructure that supports human consciousness!

In this model, DNA gives rise to human consciousness, provides a continuum, and at the end of the lifespan causes neuron degeneration.
A Neurogenetic Account of Human Consciousness

In this model, DNA gives rise to human consciousness, provides a continuum, and at the end of the lifespan causes neuron degeneration, which results in a decrease in degrees of consciousness.

This is to say, that there are 3 neurogenetic phases of human consciousness.

I will discuss these very briefly!
A Neurogenetic Account of Human Consciousness.
Phase One: The Emergence

In the first neurogenetic phase there is an emergence of neuron-based consciousness.

This begins at fertilization with master genes high in the developmental hierarchy that trans-activate other genes downstream.

There are several genes that give rise to brain regions involved in human consciousness- these are neurogenetic correlates of consciousness (NgCC).
A Neurogenetic Account of Human Consciousness.
Phase One: The Emergence

Examples of NgCC in the 1st phase:

Pax6 - master gene for eye development

Otx1 - overall size of the cerebral cortex

Otx2 - diencephalon, mesencephalon, and telencephalon development

Pax3 - acts as a master gene early in development and influences several genes, e.g., TP53, Hes1, Neurog2, and Meis2.
In the second neurogenetic phase there is a continuum of neuron-based consciousness which requires proper genetic functioning.

This can be studied objectively by observing the genetic basis of neuron plasticity and genetic abnormalities in certain psychiatric disorders, e.g., schizophrenia and autism.
A Neurogenetic Account of Human Consciousness. Phase Two: The Continuum

Examples of genes involved in neuron plasticity:

BDNF, FGF2, delta-FosB, and synapsins I-III.

Genetic abnormalities in psychiatric disorders:

Autism- PTCHD1 locus disruptions
Schizophrenia-associated genes- PDE4B, DISC1, and ZNF804a transcription factor
In the third neurogenetic phase there is neuron degeneration and loss of brain mass which leads to observable decreases in the degree of human consciousness.

Neurodegeneration can be a normal age-related process as seen in mild cognitive impairment or it can have a genetic link as seen in diseases like Alzheimer disease.
A Neurogenetic Account of Human Consciousness.
Phase Three: Neurodegeneration

Genes associated with Alzheimer Disease:
- APOE-ε4 gene variant
- APP gene mutations
- PSEN1 gene mutations
- PSEN2 gene mutations
- TREM2 gene mutations
References to the Three Neurogenetic Phases of Human Consciousness


Alzheimer Disease

Cardinal features of AD:

Memory loss - remarkably in declarative memory

Loss of cognitive skills - e.g. problem solving, language, calculation, and visuospatial perception

Behavioral abnormalities - psychotic symptoms (e.g. hallucinations and delusions) and inappropriate behaviors (due to loss of inhibition)

Progressive impairment of daily living

In later stages patients become mute, incontinent, and bedridden

Alzheimer Disease

In essence, the AD patient gradually loss degrees of human consciousness!
Eventually, they cease to be the person that they once where.
Memory and cognitive skills are lost secondary to AD pathology, which has a genetic correlation.
Alzheimer Disease

Gene mutations associated with Alzheimer Disease:

- APOE-ε4 gene variant
- APP gene mutations
- PSEN1 gene mutations
- PSEN2 gene mutations
- TREM2 gene mutations

There are many others under investigation!!!
Reference to My work on Alzheimer Disease


The Possibility of Curing Alzheimer Disease with Gene Therapy

There are several studies and trials underway in which the cure for some of the signs and symptoms of AD are being addressed with gene therapy.
The Possibility of Curing Alzheimer Disease with Gene Therapy

FGF2 transplant treatment to improve memory in Alzheimer disease.

In this study, FGF2 gene was transferred directly to the hippocampus of bigenic mice (APP+presenilin-1).

The FGF2 gene was delivered by an adeno-associated virus serotype 2/1 hybrid.

Significant improvement was seen in the mice receiving the injection at both the pre- and post-symptomatic stages of Alzheimer disease.

This was verified by testing spatial learning in the radial arm water maze test.
The Possibility of Curing Alzheimer Disease with Gene Therapy

NEU1 Gene Therapy:

The Possibility of Curing Alzheimer Disease with Gene Therapy

This study demonstrated that deficiencies of the lysosomal sialidase (which is produced by the NEU1 gene) lead to the spontaneous occurrence of an Alzheimer-like amyloidogenic process to occur in mice.

In addition, this study subsequently demonstrated that cerebral injection of NEU1 in Alzheimer-mice resulted in substantial reduction of beta-amyloid plaques.
The Possibility of Curing Alzheimer Disease with Gene Therapy

Leptin gene therapy:

The Possibility of Curing Alzheimer Disease with Gene Therapy

This study demonstrated that leptin gene therapy was able to reduce the accumulation of beta-amyloid in APP/PS1 transgenic mouse model.

In this study a lentivirus vector expressing leptin protein in a self-activating HIV-1 was delivered by intracerebroventricular administration.

This resulted in a reduction of beta-amyloid accumulation and a partial rescue of synaptic density in these mice.
The Possibility of Curing Alzheimer Disease with Gene Therapy

Other therapies involve the transplantation of somatic stem cells for regenerative therapy for several neuronal diseases.

The Possibility of Curing Alzheimer Disease with Gene Therapy

Treating the symptoms and pathology of AD with genetic therapies seems to imply enhancement.

In addition, it implies a neurogenetic connection to human consciousness.
A Neurogenetic Account of Human Consciousness and Enhancement

In the process of developing these gene therapies to cure diseases like AD are we not opening the door to the enhancement of human consciousness in people who do not suffer from AD?

This is not being discussed!

A Neurogenetic Account of Human Consciousness and Enhancement

Thank you for your “conscious” attention!!!

John K. Grandy publication list- on line articles