# Alzheimer Disease and Human Consciousness: A Neurogenetic Connection.

3rd International Conference and Exhibition on Neurology and Therapeutics.
Sept 8-10, 2014. Philadelphia, USA.

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***The International Journal of Medicine and Public Health*.**

# Alzheimer Disease and Human Consciousness: A Neurogenetic Connection.

**3rd International Conference and Exhibition on Neurology and Therapeutics.**
**Sept 8-10, 2014. Philadelphia, USA.**

**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.**

**Grandy, John. Consciousness. The Encyclopedia of Anthropology 2006. Vol. 1 (pp. 563-566). Sage Publications Inc. Thousand Oaks, California.**

# 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**

**Kandel's Principles of Neural Science, 5th edition, 2013. McGraw Hill. Page 385**

# 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.**

**Francis Crick and Christof Koch (1990). Towards a neurobiological theory of consciousness. *Seminars in The Neurosciences* Volume 2: 263-275.**

# Neural Correlates of Consciousness

**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.**

**Kandel's Principles of Neural Science, 5th edition, 2013. McGraw Hill. Page 1375**

# 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.**

**Grandy, John (2012). The Explosion of Consciousness: TSC Conference Tucson Arizona 2012. *Journal of Consciousness Exploration and Research;* 3 (4): 432-445.**

# 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.**

**Grandy, John (2012). The Explosion of Consciousness: TSC Conference Tucson Arizona 2012. *Journal of Consciousness Exploration and Research;* 3 (4): 432-445.**

# 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.**

# A Neurogenetic Account of Human Consciousness.
# Phase Two: The Continuum



**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**

# A Neurogenetic Account of Human Consciousness.
# Phase Three: Neurodegeneration



**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


**Grandy, John (2014). Neurogenetics and Human Consciousness. *The Journal of Neurological Disorders.* 2014; 2 (1). 1000e109**

**Grandy, John (2014). A Neurogenetic Account of Human Consciousness. *Essays in Philosophy.* 2014; 15 (2).**

**Grandy, John (2013). The Three Neurogenetic Phases of Human Consciousness. *The Journal of Conscious Evolution* 2013; issue 9: 1-24.**

**Grandy, John (2013). The Neurogenetic Correlates of Consciousness, in R.L. Amoroso, L.H. Kauffman, & P. Rowlands (eds.) 2013: *The Physics of Reality: Space, Time, Matter, Cosmos, 8th Symposium in honor of Jean-Pierre Vigier Singapore: World Scientific*. Chapter 48: pp 479-483.**

# 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 losses 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


**Grandy, John (2013). Melatonin: Therapeutic Intervention in Mild Cognitive Impairment and Alzheimer Disease. *Journal of Neurology and Neurophysiology* 4 (2): 1-6.**

**Grandy, John (2012). 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.***

**Grandy, John (2012). Alzheimer Disease and DNA Consciousness. *Academic Journal of Science* 2012; 1 (3): 169-184.**

**Grandy John (2011). What's new in Alzheimer Disease: Biomarkers and Gene Mutations as Aids for Detecting AD Early. *Journal of the American Academy of Physician Assistants 2011; 24(6): 56-57*.**

# The Possibility of Curing Alzheimer Disease with Gene Therapy

**There are several studies and trials underway in where 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 .**

**Kiyota Tomomi, et al. (2011).** FGF2 gene transfer restores hippocampal functions in mouse models of Alzheimer's disease and has therapeutic implications for neurocognitive disorders. *PNAS* 108 (49): E1339-1348.

# The Possibility of Curing Alzheimer Disease with Gene Therapy

**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:

**Annunziata, Ida, et al. (2013).** Lysosomal NEU1 deficiency affects amyloid precursor protein levels and amyloid-beta secretion via deregulated lysosomal exocytosis. *Nature Communications* 2013; 4:2734.

# 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:

**Perez-Gonzalez, Rocio, et al. (2014).** Leptin gene therapy attenuates neuronal damages evoked by amyloid beta and rescues memory deficits in APP/PS1 mice. *Gene Therapy* 2014; 21: 298-308.

# 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 intra-cerebroventricular 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.**

**Kanno, Hiroshi (2013).** Regenerative therapy for neuronal diseases with transplantation of somatic stem cells. *World J. Stem Cells* 2013; 5 (4): 163-171.

# 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!**

Grandy, John (2014). DNA Consciousness, Human Consciousness, and Transhuman Consciousness. [forthcoming]

# A Neurogenetic Account of Human Consciousness and Enhancement



## Thank you for your “conscious” attention!!!

**John K. Grandy publication list- on line articles**