Neuroquantum Theories of Psychiatric Genetics: Can Physical Forces Induce Epigenetic Influence on Future Genomes?

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ABSTRACT

This paper serves to encourage quantum physicists to engage in psychiatric based research on the brain and its functions (i.e., consciousness, memory, attention). By using physics theorems such as Einstein's theory of relativity and the string theory, both physicists and geneticists alike may be able to elucidate potential links between components of the universe and their effects on the human brain. We have outlined some interesting posits including the cosmos' role in evolutionary biology, alpha bonding in biological molecules, and environmentally induced epigenetic effects on genetics. We also explore how physical forces can influence human memory, behavioral traits, and rates of addiction. Impulsiveness is used to exemplify how environmental changes can contribute to epigenetics and its hereditary alterations. We propose the idea of the presence of a "mental universe," where brain functionality like consciousness is a continuum of physically altered pathways. The realization that the universe and all of its precepts remains a mystery is reflected in the lack of a standardized "unified" physics theorem and mathematical equation that can explain universal dimensions (physical and mental), and as such, so is the complex nature of the functionality of the human brain. We provide herein a suggestion to remedy possible confusion, whereby we attempt to show the relationship of brain as a complex quantum–like organ and the impact of epigenetics on behavioral expression.

Key Words: quantum physics, theory of relativity, string theory, universe, psychiatric genetics, reward deficiency syndrome, epigenetics

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Introduction

Beyond Einstein

In this paper, we are not claiming to provide pertinent mathematical solutions to the basic precept that the nervous system, especially as it relates to brain functionality, is indeed an example of quantum rules; instead, we are writing to encourage quantum physicists to further engage in in-depth scientific exploration of the emerging field "*Psychiatric Genetics*." One of us (KB) along with Ernest P. Noble, MD, PhD, published the first highly confirmed research on the association of the dopamine D2 receptor gene polymorphisms and severe alcoholism in 1990, which paved the way for many other global investigators and has now led to a total of 15,036 (11/24/2014) PUBMED published articles (Blum *et al.,* 1990). With this in mind, our team has decided to address an important scientific issue related to the *neuroquantology* of psychopathology and more specifically, gene-environmental interactions and epigenetic effects with emphasis on quantum physics. In order to do so we thought it would be useful to first discuss the fact that for most of non-physical scientists including us, we have assumed that the laws of the universe have not changed and will certainly never change.

It is implied that nature's rules are eternal, unbreakable, and all controlling. Ideas like these have

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fueled much of the physics field since Isaac Newton had formulated his laws of universal gravitation in 1687. His concepts took root approximately a century ago, when Einstein had also developed his general relativity theory. However, careful scrutiny of the so called "book of physics" and the pursuit of this truth has led to many great physics discoveries, but unfortunately has begun to seem like an unkept promise in the clear understanding of our universe. To some, the problem is that physics and all of its exacting science appears to be leading us not to resolution of Cosmic laws, but into an *"Alice and Wonderland"* world of increasingly bizarre theories far removed from our daily life experiences. Many have already proposed one interesting question: What if evolution is not only at work in biology, but also at work in the cosmos?

For many years, cosmologists have postulated that our universe is just one among an unfold number of universes that bubbles up constantly from "quantum foam". Most importantly, theoretical physicists embraced the intriguing mathematics of string theory. This theory suggests that there are seven extra dimensions besides the four we already have knowledge of. Scientists have argued appropriately that if we have to make up dimensions that have not been seen and universes that may never be found, it may be a sign that quantum physics and scientists thereof may be headed down a blind alley and as such, does one step forward actually lead us back into a "rabbit hole" in understanding nature's immutable cosmic laws?

Currently, there are a few scientists that argue the basic fundamental laws of physics and maybe it is these few that will provide new pathways for future exploration. Without extensively exploring these issues in this article, which is focused primarily on "*Psychiatric Genetics*," the following short list provides insight into this newer view:

1. Lee Smolin at the Perimeter Institute for Theoretical Physics in Waterloo, Ontario along with a non-scientist Roberto Mangabeira Unger at Harvard University, the two are collaborating on an upcoming book *The Reality of Time and the Nature of Cosmological Laws* (Frank, 2010), where they argue that the problem with theories is that they include hidden dimensions (e.g. string) and alternative universes. Unger and Smolin suggest that when we begin to imagine our universe as one out of a several possibilities, we devaluate the one we see and live in and we should try to explain that world first. This should help remind and encourage the biological psychiatrist to focus on first understanding the established candidate genes rather than seeking answers by using complex gene micro-arrays to dissect a multitude of behavioral traits. The findings of hundreds of genes either up or down regulated by a typical behavior (i.e. bipolar manic depression, major depression, Reward Deficiency Syndrome (RDS), psychosis) while interesting, must be further analyzed for which specific gene clusters and then which individual genes have significant power that contributes to the overall behavioral trait. In fact it has been recently found that a cluster of five candidate dopaminergic genes and related polymorphisms associate with depression severity symptoms (Pearson-Fuhrhop *et al.,* 2014). This is indeed the basis for polygenic inheritance. If we want to build a behavioral phenotype just like building a star in our universe (using advanced supercomputers, to simulate the complex interplay of gravity, radiation, and magnetic fields), we should at least attempt to analyze what we have observed as a behavioral trait (phenotype) rather than an imaginary trait that we cannot prove or disprove by using sophisticated imaging tools such as PET, SPECT, and fMRI coupled with genotyping. In doing so, we challenge the quantum physics community to use their mathematics and other experimental tools to evaluate the impact of how weak forces influence the atom now and in the future.

2. Stuart Kauffman, a MacArthur genius award winner and professor of biochemistry and mathematics like Smolin, does not accept the idea that the whole is understood by the expected behavior of the parts. Kauffman suggests that creativity is essentially Darwinian. He further offers that biological evolution is a powerful model for how novelty, rather than enduring laws, could play an extended role in cosmology and physics and quite possibly, just as evolutionary biology favors modification from simple to complex as observed in our universe. Most relevant to this article, from measurements of the radiation given off by distant quasars, "alpha," the physical constant that defines how tightly electrons are held to an atom's nucleus, may have been somewhat different in the early universe. As biologic scientists, we wonder whether the notion of "alpha" bonding is related to biological molecules such as proteins involved in receptor responsivity. Specifically, the polymorphic alleles that we see in brain receptors such as D1-D5 dopamine receptors have evolved; thus, the D2 A1 allele is an older or earlier version of the gene. Theoretically, carriers of this allele conferred important benefits required to survive. For example, were the hunter-gatherers blessed by having the DRD2 A1 allele, allowing for a competitive advantage in the prehistoric era? We must raise the question as to why or how do these gene polymorphisms come about in the first place and did the "alpha" constant change as an evolutionary process to cause these polymorphisms?

3. Can it be argued that something other than the past can regulate the properties of a particle in the present and this may very well be due to something that has not occurred as of yet – the future. Yakir Aharonov and colleagues at Yeshiva University in New York suggest that *time does not move in only one direction* – it is entirely possible to set up a deterministic theory of quantum mechanics. It turns out that these concepts were supported by John Howell of Rochester University, whereby, they supposedly succeeded to show that somehow the later decision (future) in their experiment appeared to affect the outcome (weak intermediate measurements), even though they were made at an earlier time (Merali, 2010). Others such as Paul Davies at Arizona and colleagues along with Alonso Botero at the University of the Andes in Colombia, have used mathematical equations to show that "bookending" the universe with specific initial and final states altering the types of particles that are created in between these states. If these and other experiments are confirmed by real experiments, could this help explain the relic radiation of the Big Bang (which has been picked up by the Planck satellite launched in 2012)? Interestingly, there are many that argue the real meaning of the Howell experiments including Andrew Jordan, who is responsible for designing the Rochester laser amplification experiment. Jordan believes that there are philosophical thoughts that limit the real value of weak measurements and if these measurements physically correlate to anything at all. Here we must ask the question - *if the future affects the past,* is it also possible that these weak forces actually impact the "alpha constant" of environmentally induced epigenetic effects of DNA structure? In essence, we are asking whether quantum physics can affect through genetic memory, as an example, inducing permanent change in future generations. This point is well researched and indeed shows the transference of epigenetic effects from generation to generation without affecting the germ-cell line (Nestler, 2011). Most recently, Byrnes et al. demonstrated that attenuated locomotor sensitization following repeated quinpirole administration occurs in F1 and F2 progeny of morphine-exposed females (Byrnes *et al.,* 2013). These behavioral effects were also observed with increased quinpirole-induced corticosterone secretion and kappa opioid receptor upregulation as well as expression of the dopamine D2 receptor (D2R) gene all within the nucleus accumbens. These results propose significant alterations in response to repeated D2R activation in female adolescent progeny exposed to opiates. Given the important role that D2R plays in psychopathology, exposure to opiates during adolescence may shift the vulnerability of future offspring to psychological disorders, including addiction. Moreover, the effects are also observed in the F2 generation, which suggest that opiate exposure during adolescence can activate transgenerational epigenetic modifications, which can impact systems vital for motivated behavior. There have been several animal studies showing that chronic cannabis smoking can lead to molecular neurobiological modifications in the reward circuitry leading to prolonged behavioral problems. This has now been confirmed by Szutorisz *et al.* (2014), who found that parental exposure to Δ(9)-tetrahydrocannabinol (THC), which is the main psychoactive component of cannabis (not the same as grown cannabis) leads to compulsive heroin seeking behavior and changed striatal synaptic plasticity in subsequent generations. Germline THC exposure was found to decrease mRNA, with concomitant reduction in NMDA receptor binding observed in the dorsal striatum of adult offspring. These results further suggest that THC exposure influences the molecular characteristics of the striatum, and can impact offspring phenotype, leading to augmented risk for psychiatric disorders in the subsequent generation through neuroepigenetic effects.

Genetic Memory: A Theoretical Posit

1. *A fundamental premise about the brain is that its functioning – also known as the "mind" – is the result of its parts: anatomy, physiology, neurochemistry, and genome. The mind, thus, is an effect of the brain and the action of its factors.*
2. *Our intent is not to argue or defend the mind/body dualism theories, but rather, understand it in terms of altering the mind's level of function. More recently, we have observed enormous massive advance in breaking the genetic code and identifying 30,000 genes found in the human genome. Current research efforts propose that evidence of recent history and biology point to a solid conclusion: that we are made up of chemically identified nucleic acids, DNA and RNA, and other functional agents such as proteins, which are either receptors or enzymes.*

If that conclusion is feasible - that we are made up of genetic material - then what differentiates us from other living organisms in this universe? Is it the "mind," or is it the evolution of our genetic material as impacted by the environment? James Payne in his book, *Doorways into the Mind,* would say that our mind is the key in terms of who we are and how we act (Payne, 2004). Or do the concepts create a hybrid of both biological and functional activity? We now understand that mutations can occur ancestrally in various genes and are then referred to as aged gene forms and there are other mutations within the same gene that can be referred to as novel gene forms. We also understand that specific environmental factors can effect gene expression, whether old or new forms.

For example, a methyl group can be added to a gene via Vitamin B12 and change its expression (Dauncey, 2014). This also true for Butyrate, a compound in research used as an anti-cancer substance extensively (Li *et al.,* 2014). These are good examples of epigenetic effects that significantly alter the genetic expression of certain genes and mRNA and miRNA transcriptional factors.

The addition of genes and the environment equals natural variation. Notice here that the genomic variation to adapt to a changing environment is a slow process that starts working selflessly for at least two generations before the inheritance of a more adaptively advantageous polymorphism; those polymorphisms can experience a non-random reversion by a process barely understood (Castro-Chavez, 2011).

Since Castro-Chavez's earlier bibliographic search entitled "*Putting Limits on the Diversity of Life,*" he discovered that variation is strongly related to homologous recombination for the generation of healthy and fertile offspring (Castro-Chavez, 2004); he also submitted an earlier article where these observations were used for practical purposes (Castro-Chavez, 2005). He concluded that "by studying the genomic compatibility of organisms we cannot only help in solving the innumerable misclassifications of the past; we can also help to reduce the currently inflated number of 'phenotypic species' by seeking organisms that are genetically compatible, to prevent their extinction and/or to generate new varieties, a fact that has been corroborated time after time in the animal sciences, crop production, and in new domestic varieties such as dog breeds (Doberman, Shar-Pei), new colorful singing birds, new semi-docile rodents, new gold-fishes, new cichlid flower horns" (Castro-Chavez, 2004).

As early as 1977, Carl Sagan in his book on the evolution of human intelligence, *The Dragons of Eden*, speculated that many compound organisms contain substantially more stored genetic and extra-genetic information than the most complex organisms two hundred million years ago (Sagan, 1977). According to Sagan, the means for attaining this information comes from "genetic memory." All organisms on have chromosomes containing genetic material passed on from generation to generation, whether they are fruit flies or human beings.

It is quite possible that a cave man ingesting *Mandragova officianarum* (mandrake root) – a psychoactive substance with extreme aphrodisiacal powers – may have experienced an effect, which passed through "genetic memory" to his offspring and later generations. The experience, which was stored as a pleasant one, may or may not be experienced later in the recipient offspring. Nevertheless, suitable extra-genetic stimuli may have triggered consciousness of that stored pleasurable experience for future generations. Given that extra-genetic triggering action (possibly certain chemicals, toxins, etc. having epigenetic effects), the recipient offspring may believe it to be a "fantasy" or "hallucination," whereas in reality, the experience may have its origin as far back as reordered history, or even as far back as the first intake of mandrake root. Do these seemingly far out theories have relevance in terms of the recent ideas of Tollaksen and others concerned with whether or not the universe has a destiny and can the future influence the destiny of any individual in terms of brain neurochemistry, genetic material, and impulsive, compulsive and addictive behaviors? (Merali, 2010).

Stringing the Theory of Relativity and Quantum Physics as Precepts for Brain Functionality

Science at times becomes far too complex with the incorporation of quantum physics. But it is much simpler than scientists let on. A particle can appear to exist in more than one state because of what some call an interdimensional event - really a fundamental property of what we already call to be time.

String theory is a plausible explanation of exactly how matter or energy and time interact with one another and what the 2 states of matter are is actually the process of vibrating between two states of matter (high and low), in which we can only measure the two 3D states that are observable. This is being done with the time component absorbed (in a four dimensional state). String theory posits that the electrons, quarks and smaller components within an atom are in a constant state of motion and the energy expelled is from the dimensional matter being transformed. These strings are able to move and vibrate, giving the particles their particular flavor, charge, mass and spin. An analogy of this for String's modes of vibration is guitar strings producing multiple, but distinct musical notes. In this analogy, the different notes match up to different particles. The only difference is that the guitar is only a 2-dimensional instrument; you can strum it up or you can strum it down. In reality, the guitar strings represent every dimension, in which the strings vibrate in any direction, showing that the particles of energy (vibrations) could move through not only our current dimension, but other available dimensions as well. As this guitar is being played, the surrounding mass (human) either enjoys the music by joining vibrational music or they do not care for the music being played and do not join in. Perhaps this is the way our cells communicate through vibrational messaging within many dimensions. Unfortunately, as the String theory suggests, these messages are being sent within many dimensions. Since we are 3 dimensional, we as conscious beings can only understand a fraction of what is being played within the vibrational symphony of the Universe.

Understanding this general concept provides the impetus to ponder whether quantum physics, especially weak forces, can actually impact our future genomes. While it is well–known that environmental motifs such as radiation can impair DNA structure, at least as a state dependent phenomenon (even possibly passed on from generation to generation epigenetically), it is not known if weak vibrational messaging can alter future generations in terms of changing important candidate psychiatric genes (DRD2, DAT1, COMT, PPAR, 5HT2a, PENK, etc.) inducing new polymorphisms, which will translate into altered behaviors (Blum *et al.,* 1997).

Physical Models of the Mind

Physical models of the mind associate consciousness with consistent superposition of states within the brain. According to some critics, consciousness can be the result of an internal quantum measurement brain process. One of the earlier concepts by Hameroff-Penrose and Tegmark suggested that the brain acted as a computer (Rosa and Faber, 2004). In fact, fifty years ago, John von Neumann contrasted the brain's structure with that of the computers he invented and are still used today. During that time, the organization of computers was rooted in concepts of brain organization (Kaiser, 2007). Reichgelt has critically reviewed the concepts related to the potential of neural networks as models of the brain (Reichgelt, 1996). Neural networks have been used to contribute alternative explanations to the symbolic descriptions of cognition within Artificial Intelligence, in which the assumption that an intelligent system has overt representation of some aspect of the world and uses these ideas in an intelligent behavior (Reichgelt, 1996). Evidently, if neural networks are considered fair models of the brain and give a satisfactory account of cognition, they could potentially become an invaluable tool in neuroscience (Reichgelt, 1996).

Copperfield's Consciousness: Now You See It, Now You Don't

According to the philosopher John Locke (1632-1704), consciousness (Latin *conscientia* or "moral conscience") is defined as the awareness of all the happenings in the human mind, whereas philosopher John Searle defined it as "inner qualitative, subjective states and processes of awareness."

In modern science, consciousness is referred to full self and environmental awareness, to the degree of in that an organism is able to respond to stimuli. Consciousness has been on the forefront of research efforts in both philosophy and natural/neuroscience because of its biological scope regarding neuronal processes and the ability for an individual to recognize oneself and its surroundings and act accordingly.

Information about conscious processing only appeared during the mid-20th century, where many functional networks were arranged in order to cooperate with one another as neuronal substrates. Moruzzi and Magoun found that the ascending reticular system (ARAS) is composed of the mesencephalic formatio reticularis and its projections to the thalamus, with patients suffering from impaired consciousness providing further details (Moruzzi and Magoun, 1995).

The mesencephalic ARAS projects 1) via the reticular thalamus to the cortex, 2) via the hypothalamus to the basal forebrain and limbic system, and 3) via the brainstem and locus coeruleus as well as their cortical projections. The reticular system is motivated by several somatic and sensory pathways and behaves as a lead controller for cerebral cortex neuronal activities.

The main role of the ARAS is to center our attention on particular stimuli or internal processes, which function via neuronal groups and several neurotransmitters responsible for states of consciousness and wakefulness. ARAS stimulation creates an arousal response as the electric correlate of consciousness; damage to it can cause either coma or closely related states. The most prominent levels are cortical (prefrontal and association) recognition networks, motor activity, long-term memory and attention, with the left hemisphere as dominant. Various levels of consciousness are evident: 1) normal level of consciousness, 2) coma, 3) Vegetative state, and 4) minimally conscious state. These levels occur because of damages in functionality regions of the brain, either by psychogenic factors or experimentally, and are joined by neurological and psychiatric disorders.

Cognition: Learning Bit by Bit

Since Golgi and Cajal are responsible for the identification and mapping of brain neuronal circuits, neuroscientists asked pressing questions about brain functioning: *"How do neurons communicate with each other in a network? Is there some basic principle according to which brain networks are organized? Is it possible to map out brain regions specialized in carrying out some specific task?"* (Agnati *et al.,* 2007). Considering the first question, it is popular belief that both Golgi and Cajal had opposing views on the interneuronal communication. Golgi believed in protoplasmic continuity and/or electrotonic spreading of neuronal currents; Cajal, on the other hand, introduced the "neuron doctrine," in which neurons communicate via the synapse. We ponder how different frequencies induce differential release of neurotransmitters and as such, this is another area where quantum physicists can participate and help move psychiatry forward. Can nanotechnology be utilized to explore potent molecules with specific

electrical charges to mimic the exact frequencies required to release neurochemicals in the synapse? Can water be utilized as a nano carrier of elements?

One of the major components of neuropsychopharmacology is neurotransmitter mapping and it also serves as a reference for the biochemical and behavioral examinations of brain functioning. Biochemical techniques have allowed for numerous transmission lines in synapses communicating via receptor-receptor interactions built from supramolecular aggregates, or receptor mosaics. The Agnati-Fuxe teams have introduced the concept of volume transmission by using immunocytochemical and autoradiographic mapping, which led to the observation of extra-synaptic receptors and of transmitter-receptor mismatches leading. The concept of volume transmission explains three-dimensional diffusion (e.g. of transmitter and ion signals), which can be released by any cell, either in extra-cellular space or the cerebrospinal fluid of the brain. Hence, a combination of Golgi and Cajal's ideas were made possible, by suggesting two modes of intercellular communication: volume transmission (VT) and wiring transmission (WT) (an example of the latter is synaptic transmission) as well as two networks (cellular and molecular) in the central nervous system. This theory is the foundation for brain morphological and functional organization concepts, such as the miniaturization and hierarchic organization. Finally, there has been a new proposal for a model of brain networks, in which a *"network of fibrils enmeshes the entire CNS forming a global molecular network (GMN) superimposed on the cellular networks that could impact consciousness as well other mind-brain events"* (Agnati *et al.,* 2007).

Most interesting is the work by Fuxe and associates exploring new models of brain function. These theories may shed light on novel therapeutic targets to influence mind-brain functionality (Agnati *et al.,* 2007). In one example, it was found using highly complex quantum related methodology that the affinity of D2 receptors for agonists is reduced by homocysteine, which behaves like an allosteric D2 receptor antagonist, but this is not the case for antagonists. Mass spectrometry illustrates homocysteine forming non-covalent complexes with two Arg-rich epitopes of the third intracellular loop of the D2 receptor, in which one is involved in A(2A)-D2 receptor heteromerization via an arginine (Arg)-thiol electrostatic interaction (Agnati *et al.,* 2006). Fuxe's group present important evidence that G-proteins and its allosteric control of G-protein coupled receptors may be therapeutic targets for development of novel substances having biological activity at plasma membrane grouping of receptors in receptor mosaics (high-order receptor oligomers) and their importance to networks related to gene controlled plasma membrane domains. Given that our laboratory has done research on neuropsychiatric genetics of addictive behaviors (e.g. alcohol, cocaine, etc.), especially dopamine D2 receptor polymorphisms, it is of great interest that Fuxe's group has recently concentrated on the important interaction of the adenocine [A2A] and the Dopamine D2 receptor (Blum *et al.,* 1990; Noble *et al.,* 1991; Noble *et al.,* 1993; Blum *et al.,* 2009). In a paper, they used Atomic Force Microscopy on immunogold arrangements of A2A and D2 receptors in CHO cells and data obtained by means of computer-assisted confocal laser microscopy (quantum physics methodology) and suggested that alterations in D(2) and A(2A)-D(2) trafficking induced by allosteric actions of cocaine at D(2) receptors may potentially add to the D(2) signaling changes often seen in cocaine abusers (Genedani *et al.,* 2010). The importance here is that through the use of quantum physics related measurements, our scientific opportunities are increasing. A case in point is using sophisticated techniques they are able to pin-point genetic mutations. Thus, their results indicate specifically that by "targeting A(2A)R serine 374 it will be possible to allosterically modulate A(2A)R-D(2)R function, thus representing a new approach for therapeutically modulate D(2)R function" (Borroto-Escuela *et al.,* 2010).

There are numerous studies on social cognition and even gene–environment interactions involving political partnering, being a republican or a democrat, and friendship and attachment as reported in the studies of Fowler et al. relative to dopaminergic genetics (Fowler *et al.,* 2009; Fowler *et al.,* 2008). While neuroimaging studies associate medial rostral prefrontal cortex (mrPFC) in self-referential processing, simulation studies of social cognition propose that this region is also responsible for thinking about others. Benoit et al. predicted that mrPFC may be a causal factor for praising the personality traits of another person to the degree that this person is reminded of oneself (Benoit *et al.,* 2010). Functional MRI (fMRI) was used while two factors were crossed: 1) utilizing memory judgments and expression of personality traits or characteristics and 2) the reference for these judgments (e.g., oneself or another individual). The study outcome shows that mrPFC haemodynamic alterations are present in personality and memory retrieval judgments about oneself. There was also a correlation with judgments about others, indicated by the BOLD signal in this particular region. In addition, those subjects who thought they were more like their friends in terms of traits had greater trouble trying to remember judgments in terms of themselves or their friends. This result was observed in the mrPFC BOLD signal as a correlation between self and friend judgments and the use of memory to refer to such judgments. Results such as these propose that mrPFC activity during self/other judgments should refer to the psychological similarity effect (Benoit *et al.,* 2010). In fact, our laboratory has also shown the relationship between

marrying a partner who carries similar genotypes for the dopamine D2 receptor gene and this may impact one's happiness (Blum *et al.,* 2009; Blum *et al.,* 2012). Fröhlich proved that a set of oscillators is able to compact full of energy, which is responsible for the activation of the vibrational mode of the lowest frequency in 1968. This principle is closely compared to the Bose-Einstein condensation, superconductivity, lasing, and other macroscopic quantum coherence properties. Moreover, Fröhlich condensates are classified into 3 types: 1) weak condensates, in which profound effects on chemical kinetics are possible, 2) strong condensates, where large masses of energy can be turned into 1 vibrational mode, and 3) coherent condensates, in which the energy is channeled into 1 quantum state. Coherent condensates have high energy states, so they cannot be made by the Wu-Austin dynamical Hamiltonian because its energy is too low and they cannot be replicated in a biological environment. Because of this, Hameroff-Penrose created an objective-reduction model and theories for cognition that represent Fröhlich's coherent condensation, but these efforts are rather unsound. Nevertheless, weak condensates may have significant effects on kinetics, and may potentially have the ability to be created from biochemical energy or from radio frequency, microwave, or terahertz radiation. Sources for such energy can be taken from Pokorný's 8.085-MHz microtubulin or possibly from microwave reactors (green chemistry) and terahertz medicine (Reimers *et al.,* 2009).

In terms of genetic influences on cognitive ability, there have been some findings. By studying 2,091 Scottish people, researchers found that carriers of the DRD2 A1 allele had lower generalized cognitive ability ("G" score) than A1 negative carriers (Bolton *et al.,* 2010). This takes on importance when we consider the role of decision–making and "recall" especially at the Pre-Frontal Cingulate and its resting state connectivity with the NAc region of the brain. It has been also been found that carriers of the DRD2 A1 allele are poor "recall" processors and this has real relevance to drug seeking relapse (Blum *et al.,* 1996; Dahlgren *et al.,* 2011). Moreover, using PET scan analysis of 230 adult patients with mild cognitive impairment (MCI), 18.7% were hypo-metabolic (n=43) and 81.3% were normal (n=187). Those with brain hypometabolism including amnestic or non-amnestic MCI, had significantly (ANOVA) slower P300 brain processing speed (346.7ms, p=0.00006) and lower voltage (3.5mV, p=0.003) than patients with normal PET results (327.5ms, 4.7mV) (Braverman *et al.,* 2013).

Epigenetic Implications Modulating Impulsiveness: A Case for Strong or Weak?

Epigenetics includes hereditary alterations in the genome without necessarily changing DNA sequences, which is comprised of 1) gene expression crossing over cell generations, 2) alteration of gene expression during cell differentiation, and 3) environment-induced alterations of gene expression. Despite the maintenance of these changes over the cells' generations, there remain no changes to the DNA sequence, but instead non-genetic factors induce genes to "express themselves" differently (Reik, 2007). Transgenerational epigenetic inheritance occurs in gene-environment interactions in many different species (Jablonka and Raz, 2009; Nadeau, 2009; Vandegehuchte *et al.,* 2010). Neuropsychiatric disorders and early expression of epigenetic consequences occur due to abnormal fetal and early life conditions responsible for disrupting normal brain growth (Archer, 2010; Archer *et al.,* 2010; Waterland *et al.,* 2006). Early life issues mainly affecting adolescent and adult behavior occurs because of epigenetic mechanisms that are caused by environmental influences and result in chronic disease states (Gomes and Waterland, 2008; 2009). Specific expression of disorders (e.g. psychosis) integrate the connection between childhood issues and disease states along with epigenetic stress regulating functions of the hypothalamic-pituitary-adrenal axis and the neurobehavioural mechanisms responsible for early life trauma that may potentially cause psychotic experiences (Read *et al.,* 2009); drugs can be used for treatment, but may also modify the genome (e.g., DNA methyl transferase inhibitors and histone deacetylase inhibitors) for such issues, emphasizing the necessity of epigenome targeting (Narayan and Dragunow, 2010). Epistasis occurs when one gene is altered by one or more "modifier" genes; epistatic gene phenotypes are expressed, while hypostatic gene phenotypes are altered in some way according to the strength and kind of epistasis - an important determinant of disorder propensity (Priest and Wade, 2010). Epistasis gives evidence for mechanisms during etiopathogenesis of neurobehavioral attributes (e.g. neuropathological impulsiveness), which support the development of neuropsychiatric disorders (Montag *et al.,* 2010; Wells *et al.,* 2010). *Endophenotypes* as neuropsychiatric concepts and biomarkers follow the pathway between gene to disorder, which is correlated to expressed mutations that are observed in unaffected relatives, vulnerability polymorphisms, and the cognitive-emotional regions (Turetsky *et al.,* 2008). Contributions of endophenotypes and epistasis may help better diagnosis practices, intervention methods and final prognosis (Archer *et al.,* 2010).

Issues during childhood and adolescence can affect essential brain development (Waterland *et al.,* 2006), with maternal care influencing hypothalamic-pituitary-adrenal (HPA) stress reactions through specific gene transcription and epigenetic regulation effects of glucocorticoid receptor expression (de Kloet *et al.,* 2009; Weaver, 2009a; Weaver *et al.,* 2004). Social and environmental stress during childhood and

adolescence (e.g., abuse, neglect, poverty, and poor nutrition) are correlated with increased rates of mental and physical illness (e.g. anxiety, mood disorders, poor impulse control, psychosis, and drug abuse). Weaver (2009b) explains results from several studies elucidating the relationship between childhood and adolescent experiences (including parent-infant bonding), hypothalamus-pituitary-adrenal axis activity, brain development, and health outcome can help explain how neurobiological mechanisms that control stressors that affect personality development and the initial stages of illness. Changes in HPA stress reactions result in increased risk for neuropsychiatric disorders such as emotional dysregulation, cognitive inadequacy and impulsiveness (Dedovic *et al.,* 2009; Preussner *et al.,* 2010). McGowan *et al.* (2009) observed epigenetic variations in a glucocorticoid receptor (*NR3C1*) promoter between the hippocampus taken from suicide victims with positive/negative childhood abuse (e.g., sexual contact, severe physical abuse and/or severe neglect; n=12), compared with other suicide victims, who did not experience childhood abuse (n=12), and controls (n=12). They obtained, in the childhood-adversity suicide victims, decreased levels of glucocorticoid receptor mRNA, lowered mRNA transcripts containing the glucocorticoid receptor 1_F split variant and boost cytosine methylation of an *NR3C1* promoter. These authors showed too that patch-methylated NR3C1 promoter compositions that copy the methylation of childhood stressors suicide victims' samples expressed decreased NGFI-A transcription factor binding and NGFI-A-inducible gene transcription. Similarly, HPA axis activity control and hippocampus-linked cognitive functioning requires reflection: Khalili-Mahani *et al.* (2010) conducted a functional MRI study comparing stress-responders and non-responders by utilizing efforts that directly affect hippocampal formation. The former had observed variations in hippocampal activity before stress, with increased activity and cortisol while cognition is used, signifying that hippocampal activation before stress may show increased vigilance or anxiety states. Canli *et al.* (2006) investigated neural correlates of epigenesist, indicating that childhood and adolescent stress affects serotonin transporter genotype on amygdala and hippocampus resting activation, thus regulating stress levels (Graff and Mansuy, 2009). Quirin *et al.* (2008) have observed that the HPA system and hippocampus are set up during development periods, creating a specific timeline of physiological reactions throughout one's life course. Lahiri *et al.* (2009) have also suggested a "latent early-life associated regulation" (LEARn) representation, in which underlying alterations in the expression of developmental genes primed initially during development with environmental events disturbing, epigenetically, at long-term regulation, from the early-life stages, but involving perturbations that only produce a neuropathology later in the life-cycle. Therefore, genetic and environmental risk factors add to the etiopathogenesis of brain disorders, in which symptoms are influenced by dysregulation during the control of impulsiveness (Palomo *et al.,* 2007).

Impulsiveness included a range of multiple inter-related factors that consist of reward-seeking and reckless behaviors, lack of planning and self-control, with or without aggressiveness, that have associations with various psychopathologies (Haden and Shiva, 2008; Palomo *et al.,* 2007; Reynolds *et al.,* 2006). Regression analyses based upon several self-report questionnaire studies, which also incorporate an array of cognitive-emotional traits, have shown that impulsive behavior is validated by many negative effects, such as amotivation and depressiveness, and is counter predicted by positive effects, such as self-control in normal adult populations, including students and adolescents (Palomo *et al.,* 2008a, b; Miller *et al.,* 2009). The inability to make decisions based on future events shows a significant element of impulsive behavior expressed in men classified as both non-psychopathic and psychopathic (Dolan *et al.,* 2002), euthymic and depressed bipolar patients, depressed unipolar patients, those patients who are healthy (Peluso *et al.,* 2007), and male psychiatric in-patient criminal offenders (Haden and Shiva, 2008). Those who have increased impulsive behavior are observed to have more impairments during neurocognitive tasks such as executive functioning tests (Dolan and Park, 2002; Keilp *et al.,* 2005; Rogers, 2003), response control tasks (Harrison *et al.,* 2009; Potter and Newhouse, 2004), and cognitive flexibility or verbal fluency (Barratt *et al.,* 1997; Vieregge *et al.,* 1997). Self-control is regulated largely by the eventual consequences of affective (cognitive) appraisals along with reinforcement/avoidance controlled by principal neural circuits (Beck *et al.,* 2009; Frank and Claus, 2006; Koenigs and Tranel, 2007; Rustichini, 2005). Functional gene variants have implications on neural mechanisms of impulsiveness disorders, including serotonin transporter gene 5-HTTlPR functional variants (Racine *et al.,* 2009; Silva *et al.,* 2010).

Serotonergic systems are involved in neuropsychiatric disorders (Lowry *et al.,* 2008) and regulate the functional domains of cognition and emotion (Murakami *et al.,* 2009). Both impulsive and aggressive behaviors are related to serotonergic system functioning (Lee and Coccaro, 2001; Zouk *et al.,* 2006), which are sometimes considered attributes associated with genetic structures that are made further complex by epistasis (Pezawas *et al.,* 2008), epigenesis (Philibert *et al.,* 2007; Philibert *et al.,* 2008), gender moderation and ethnicity (Williams *et al.,* 2003). Benko *et al.* (2010) used the Impulsiveness Subscale (IVE-I) of the Eysenck Impulsiveness, Venturesomeness and Empathy Scale and the Barratt Impulsiveness Scale (BIS-11) for 725 healthy Hungarian subjects (129 males and 596 females) to

examine the relationships between the C(-1019)G functional polymorphism, HTR_{1A} gene expression, and impulsive behavior. There were observed differences between the C(-1019)G genotypes, GG vs GC vs CC: GG types had much higher motor and cognitive impulsiveness on the IVE-I scale and high total impulsiveness scores on the BIS-11 scale. The authors suggest that the expression of the receptor gene, HTR_{1A}, is a particular phenotype for impulsiveness. Several other studies have shown correlations between serotonergic gene polymorphisms, hazardous health behaviors and impulsiveness (Stoltenberg *et al.,* 2008). Stoltenberg and Nag (2010) used a mathematical representation of genetic control of presynaptic serotonergic function and genotyping of the TPH2 intron-8 (rs1386483) polymorphism and the MAOA u-VNTR amplification to explain the negative relationship between simulated levels of CSF-5HIAA levels and BIS-11 total scores in a Caucasian (95%) student population (N= 200, 62% female). Pathological gambling, risky-choice behavior and faulty decision-making due to impulsiveness are all associated with alterations in serotonergic functioning (Murphy *et al.,* 2008; Walderhaug *et al.,* 2002; Walderhaug *et al.,* 2007; 2008) and alterations to 5-HT transporter 5HTTLPR polymorphism (Jollent *et al.,* 2007; Must *et al.,* 2007). Juhasz *et al.* (2010) observed the TPH2 haplotype of the TPH2, TPH1, SLC6A4 and HTR1A serotonergic gene polymorphisms were correlated to risk behaviors assessed with a probabilistic gambling task in a population cohort of 1,035 subjects. They found that carriers of TPH2 had decreased risk-taking on cognitive tasks that contained no association between the functional polymorphisms in the TPH1, SLC6A4 and HTR1A genes and risk behavior. Despite the marked in-roads to gene-marking in both patient and healthy volunteer patients, the genetic associates between impulsiveness and the methods that assess this behavior, as well as the serotonergic pathways propose the connection, rather than the full participation in this particular condition.

Issues regarding behavioral inhibition, including impulsiveness, aggressiveness, and substance use disorder seem distinctive to several disorders such as attention deficit hyperactive disorder (ADHD) and borderline personality disorder (BPD), which involve impaired neuropsychological functioning and emotional dysregulation (Lampe *et al.,* 2007; Blum *et al.,* 1997; Blum *et al.,* 1995). Reif *et al.* (2006; 2009) have observed a polymorphic promoter dinucleotide repeat length variation of the *NOS1* gene (*NOS1* Ex1f-VNTR), which may potentially be related to clinical characteristics of impulsive behaviors (Reif *et al.,* 2009). Retz *et al.* (2010) have examined the association between self-reported impulsiveness, venturesomeness and empathy in 182 adult males (young to middle-aged) Caucasian offenders referred to forensic psychiatric medicine; impulsiveness and venturesomeness presenting closely related facets (Eysenck *et al.,* 1990) and empathy involving moral reasoning, prosocial behavior and control of aggression (Eisenberg, 2000; Eysenck *et al.,* 1990). They found that impulsive behavior correlated significantly with NOS1 Ex1f-VNTR and violence and childhood ADHD symptoms; while, venturesomeness only had a strong tendency to impulsive behavior. Empathy also correlated significantly with NOS1 Ex1f-VNTR, but not with violence or childhood ADHD. Jacob *et al.* (2010) investigated interactions of serotonergic candidate genes (5-HTT, HTR1A, and TPH2) compared with burdensome life experiences of 183 patients who have personality disorders and 123 patients who have adult ADHD. Only the G allele of HTR1A rs6295 had increased the risk for emotional-dramatic cluster B personality disorders, but also increased the risk for anxious-fearful cluster C personality disorders, thus demonstrating that the gene effect can be altered by life stressors. Not all disorders related to serotonergic candidate gene interactions (e.g. ADHD) have symptoms such as impulsiveness: Johansson *et al.* (2010) used a Norwegian sample of 451 adult ADHD patients and 584 controls along with a meta-analysis of a sample of 1,636 ADHD cases and 1,923 controls to genotype-tag variants within TPH1 and TPH2 genes, but these results revealed a failure to link common genetic variants on ADHD. Nikolas *et al.* (2010) performed a linear regression analysis on a cohort of 404 adolescents and found 5HTTLPR x self-blame interactions for ADHD symptoms, suggesting that altered serotonergic activities can be considered risk factors for ADHD when including signs of psychosocial distress in relation to inter-parental conflict. ADHD is a prominent topic because of its range of neurodevelopmentally-inappropriate attention issues, motor hyperactivity and impulsive behavior that occur during childhood often with changes in social and academic functioning. Perinatal stress or infection and/or maternal affective disorder which are important in developing attachment affect epigenetic mechanisms expressed in lengthy alterations to the HPA axis (Franc *et al.,* 2009). Expressed in ADHD and other disruptive disorders, emotional dysregulation (Martel, 2009) advances through epigenesis from temperamental difficulties in infancy to impulse control issues during childhood and later to substance use, with comorbid aggressive-impulsivity (Harty *et al.,* 2009) in adolescence and finally more severe substance abuse and criminal behavior in adulthood (Lahey *et al.,* 2005; Tarter *et al.,* 1999). We have most recently, raised the question as to when genotyping the young is parsimonious in terms of ADHD risk alleles (Gold *et al.,* 2014).

Taken together, there are several avenues implicating epigenetic mechanisms in pathological impulsive behavior found in neuropsychiatric disorders that link not only serotonergic and dopaminergic (Ponce *et al.,* 2009) systems, but also

MAO-activity and COMT (Hoenicka *et al.,* 2010) genes and even Neuropeptide Y gene (Lesch *et al.,* 2011) in the disease etiopathogenesis. As yet, one may only assume that the relative 'weakness' or 'strength' of the forces inducing epigenetic modulations of future genomes that influence impulsiveness may regulate outcomes of linkage studies. It is a great possibility that epigenetic mechanisms need further research and evidence and we could only guess as to the importance of *neuroquantology* in addiction seeking behaviors.

The Mental Universe

The human brain's modalities may indeed prove to be part of a realm of infinite functional states, as neuronal interactions produce numerous altered physical and conscious states. Analogous to the idea of multiverses and "pocket universes," there could in an infinite number of mental functional states with finite properties. Functional states, created from physical processes like electrical conduction in the brain, may be indicative of physical-mental interactions wherein consciousness is a continuum of physically altered pathways. Iterations of these events are similar to the causality space-time events in which occurrences are consistent in multiple dimensions. In this sense, the brain can be thought of as a universe or multiverse-like realm where events are dictated by realities in its physical structure across dimensions.

This idea is echoed in Spinoza's monism, when he theorized that the mind is an idea of the body as espoused by Payne (2004). Minds are seen as expressions of bodies (physical states) to which they correspond mentally. The mind is therefore a complex composite of many simple states that act and are acted upon. Spinoza's idea of the mind is consistent with his substance monism, which claims that there is one single reality, or substance. According to Spinoza, God and Nature are part of the same reality and the fundamental substance (everything) is the basis for the universe and of which lesser modes or modifications (subsets of the fundamental substance) are determined to exist by complex interactions (Dutton, 2014). However, when we consider the concept of the "*mental universe*" (developed by co-author ML), we must also consider the ideas of Hawking (1988) that the universe is infinite, whereby it has no beginning or end. Understanding this simplistic idea raises the question of whether or not so is the power of our brain as also being infinite (Rucker 1982). In our view, based on our biological knowledge of procreation, there must be a beginning and at death, an end. Thus, in reality, we suggest disconnect between the universe and our mental status or functional brain. This does not negate the ever-changing interaction of our universal environment (epigenetics) and neurotransmission of our brain.

Conclusion

As clinicians, treatment professionals, neuroscientists, psychiatrists, academicians, geneticists and neuropharmacologists, this enormous task of trying to combine neuropsychiatric genetics with quantum physics seemed unconceivable and not worth the exploration. Over the last few years, quantum mechanics has made a major impact on deciphering what role it plays in the consciousness and the power of the mind. On one side of this debate stands: conservative neuroscientists who believe that brain science begins with the neuron and candidate genes regulate neurotransmitter signaling, and on the other side are biological minded physicists, who believe that quantum physics may play some role in consciousness of the mind. Nevertheless, one cannot separate both consciousness and mind into single entities. The submicroscopic world of the human brain gives rise to consciousness and the mind. There are others such as James Payne who believes that the brain controls the workings of the mind with very distinct rules. For the most part, scientists find difficulty in distinguishing between mind and matter. Hence, there is no "mind" that is different from "matter" and no "matter" that is different from "mind." The brain is considered by some to be a physical system composed of a mixture of macroscopic and microscopic neuron systems. The macroscopic system is made up of pathways of neural impulses. The microscopic system is responsible for the body interacting with the macroscopic system. This proposed integration has been missing a very important piece of the puzzle: the intricate relationship of genes, environment and their subtle induction of behavior and learning. We now ponder the question as to the powerful interaction of genes (DNA) *x* environment (epigenetics) and the future of "*Psychiatric Genetics*" our genomes and the quantum influences seen or unseen that could change our world and universe "relativity".

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