THE EVOLUTION OF ADDICTION TREATMENT: THE DISEASE IS RDS AND ADDICTION IS ITS SYMPTOM

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ABSTRACT

The science of neurogenetics offers a new theoretical model of addiction, defining Reward Deficiency Syndrome (RDS) as the phenotype of addiction. This model appears to be a perfect fit for understanding cocaine use disorder and the complexity of it"s neurological challenge. Decades of research have resulted in a vast evidence base in support of RDS, which is now inspiring research of RDS solutions. A new science of relapse is exploring the molecular, cellular and neurological processes of craving, drug seeking, and relapse in nonhuman samples. Results inspire hope for the future of recovery through neurological intervention to reset brain imbalances and disrupt the neurotransmission of relapse.

KEYWORDS: Molecular, cellular and neurological.

INTRODUCTION

Enlarged perspective garnered from many sciences, contribute to the advancement of the evolving Bio-Psycho-Social Model of addiction-treatment (Guillemin & Barnard, 2015; Ghaemi, 2009; Borrell-Carrio, Suchman & Epstein, 2004; Engel, 1981). However, still there is no unified, comprehensive model of addiction and/or psychological theory from the last century, which comes close to explaining cocaine addiction's complexity and neurological impairment (Henriques, 2015; Hunt, 2014). Some sufferers have described it as soul cancer.

In 2011, The American Society of Addiction Medicine provided more clarify and established a more formal definition of the disease, stating in press that "addiction is a primary, chronic disease involving brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social, and spiritual manifestations (Smith, 2011). Practitioners from many sciences have attempted to define addiction, characterizing the disease according its expression within the realm of their field of interest. However, outward expression is symptomatic not causative. For example, addiction is psychologically characterized by disruptions in motivation to meet basic needs, while increasing using behaviors. This description negates the influence of neurogenetic processes which precede psychological and behavioral expression.

DISCUSSION

In true reductionist fashion, neuroscientists have explored genetic precedents and created explanation for neurological response patterns of the disease process. Decades of research from the field of neuro-genetics (Alguacil & Gonzalez-Martin, 2015) have provided the foundation for the theoretical suggestion of a new phenotype of addiction, Reward Deficiency Syndrome, which manifests in compulsive, impulsive, and addictive behaviors (Blum, Braverman, Holder, et al, 2000; Blum, Gold, Liu et al, 2011a).

As RDS, redirects focus away from older addiction models, it ignites a plethora of new research in search of RDS solutions. Having identified polymorphic variances which contribute to predisposition, a gene panel map can be used to determine risk. Genetic Addiction Risk Score (GARS) prescreening is now available (Blum, Oscar-Berman, Demetrovics et al, 2014; Blum, Braverman, Chen et al, 2008; Blum, Cull and Sheridan, 1995).

Cocaine is a strong central nervous system stimulant that increases levels of dopamine, associated with pleasure, and movement in the brain's reward circuitry. Normally dopamine is released by a neuron in response to a pleasurable signal and then recycled back into the cell that released it, thus shutting off the signal between neurons. Cocaine acts by preventing the dopamine from being recycled, causing excessive amounts of the neurotransmitter to build up, amplifying the message and effector protein response, ultimately disrupting normal

communication (Blum, Chen, Giordano, 2012a).

With habituation, some develop sensitization, tolerance and neuroadaptation as repetitive neural loops are engrained by experience. These neural pathways can be reactivated by cue inducement, operating beneath the level of conscious, initiating relapse on the molecular and cellular levels. Atypical patterns of brain wave activity become embedded and encoded into neural circuitry.

Dopaminergic dysregulation and imbalance created by self-administration of cocaine are met with the brain's responsive attempt to regain stability and balance by adjusting the dopaminergic set point, creating a new below normal for dopamine neurotransmission (Blum, Bowirrat, Carnes et al, 2012b). Early dopaminergic system research established that deficits of the DRD(2) receptor and the DRD(2) A1 Allele predispose individuals to a high risk for multiple addictive, impulsive and/or compulsive behaviors (Bowirrat, & Oscar-Berman, 2005; Blum, Gardener, & Oscar-Berman, 2012b). "Activation instead of blocking mesolimbic dopaminergic reward circuitry is the preferred modality in the long term treatment of RDS" (Blum, Chen, Chen et al, 2008).

In addition to dopaminergic systems, Cocaine, a triple reuptake inhibitor, also disrupts serotonin and norepinephrine reuptake inhibitors, confusing receptor perception and effector protein response. Research has determined that a "molecular profile of cocaine abuse includes the differential expression of genes that regulate transcription, chromatin and dopamine cell phenotype" (Bannon, Johnson Michelbaugh et al, 2014, p. 2191). This type of research may one day identify a unique neurological signature or biological marker of cocaine addiction.

Cocaine self-administration shows remarkable resistance to extinction (Weiss, 2001). Additionally, in the specific case of cocaine, drug seeking behavior can actually progressively increase in strength, incubating during abstinence (Grimm, 2001). Cocaine reinstatement is a product of molecular and cellular processes which intensify craving and increase drug seeking on a neurological level. It has been hypothesized that increases in drug use are caused by decreases in dopamine signaling within the Stratium, as such researchers are exploring the possibility that restoring dopamine signaling in the Stratium might therefore reduce drug use (Willuhn, Burgeno, Groblewski, et al, 2014). Results found that L-DOPA increased dopamine release in rat studies.

Polymorphism, or gene variance alone, does not cause addiction. Hypo-dopaminergic trait genes combined with the interaction of environmental influences determines outcome of Reward Deficiency Syndrome, which can manifest in addictive behavior, and contributes a spectrum of dopaminergic disorder, such as depression, Autism, Asberger, Azheimer, and Parkinson's Disease. The complex interactions between genetic material and environmental influences (Enoch, 2012) induce epigenetic pressure, which result in RNA recoding DNA (O'Brien, 2008).

While science has not yet discovered the exact cause, it has simplified the RDS process of neurological dysregulation which plays out in addiction. The RDS model works perfectly for cocaine addiction. Although currently without a great deal of research support, it has been suggested that other drug addictions and the process behavioral addictions may also fit neatly under the RDS umbrella. Blum would like to establish a common neurogenetic diagnosis for all addictions under the RDS rubric (Blum, Febo, Bafgaiyan, et al 2017), based upon the presence of Meso-Limbic manipulation of hypodopaminergic function. He has been marketing this idea in publication for the past few years (Blum, Febo, McLaughlin, et al, 2014).

Pharmacological and pharmacokinetic research contribute enlarged perspective of addictive variables which may induce neuro-adaptation. Pharmacokinetic research has provided understanding of individual metabolism rates and processes of biotransformation, which effect bioavailability of dosage. Routes of substance delivery, intensity of dosage, frequency, intermittency and reinstatement patterns all effect neurological consequence.

Meta-analysis suggests "how fast" and "how often" may be more important than "how much" (Allain, Minogianis, Roberts, et al, 2015). "Temporal patterns of cocaine intake determines tolerance versus sensitization of cocaine effects at the dopamine transporter" (Calipari, Ferris, Zimmer et al, 2013, p. 2013). Animal studies may lead to clinical human study. However, the design of these studies does not accurately reproduce the range of human administration patterns, so results should not be interpreted as generalizable to human populations.

Repetitive exposure to cocaine dysregulates dopaminergic, serotonergic and norepinephrine systems, initiates neuroadaptations which increase craving and reinstate relapse. Understanding the pharmacokinetics of drug use, and the pharmacological consequences of cocaine use in particular, will prove to be helpful in developing molecular and cellular pharmacological interventions to assist in dopamine restoration and rebalance other neurotransmitters such as norepinephrine which is known to help regulate withdrawal and assist in abstinence and glutamate which is associated with intense craving and cue-induced reinstatement.

To further understand structural and functional neuroadaptations caused by repetitive self-administration of cocaine, researchers studied norepinephrine systems in nonhuman primates, conditioned for self-administration

but now forced to abstain, to check for any changes in the artificially induced increases in norepinephrine levels seen after repeated exposure, to find that there was no difference in norepinephrine levels of abstaining populations and control animals (Smith, Beveridge, Nader et al, 2016). This line of research may someday lead to pharmacological intervention for humans.

Research study design neuroimaging nonhuman subjects reviewed functional brain activity in response to cue reinforcement to find that increased glucose levels before self-administration, decrease after self-administration. This increase is interpreted as being associated with human addiction neuroadaptations (Porrino, Beveridge, Smith et al, 2016).

Another study performed rat brain tissue analysis of the role of Neurokinin-I receptors suggests it mediates alcohol seeking in response to cue activation for addicted rats but was not significant in mediating cocaine seeking. Interesting results showed no effect upon non-addicted, nongenetically predisposed populations. This study may be helpful in future pharmacological studies which explore NK1R antagonists utility in treating cocaine use disorders (Schank, King, Cheng et al, 2014).

Building upon the correlation between increased glutamate release in the NAc, upon cue presentation, and the resulting increase in cocaine-seeking, researchers designed a study which explored the mediating effect of increasing mGluRi transmission, finding that mGluRi receptors in the NAc "negatively regulated CP-AMPAR levels, and thereby reduced cue-induced cocaine craving" (Loweth, Scheyer, Milovanovic et al, 2014, p. 78), in rats. This study's results suggest that mGluRi PAMS should be explored in future research design as possible pharmacological intervention to reduce craving in human subjects.

Perhaps one of the more anticipated future contributions from pharmacological research is the creation of a new line of antidepressants, which function as triple reuptake inhibitors and mimic cocaine's effect upon on dopaminergic, serotonergic and norepinephrine systems. Results from European neuro-scientist B. P. Guiard's study of the "electrophysiological properties of triple reuptake inhibitors on monoaminergic neurons" (Guiard, Chenu, El Mansari, et al, 2011, p. 211) offer evidence-base support for the similarity of pharmacological process in synthetic substitutes for commonly abused drugs like cocaine, in rat populations. By exploring potential dopamine expression by synthetic cocaine replacement therapy in rat populations, Guiard anticipates gaining insight into human response, hopefully resulting in human pharmacotherapy interventions (Guiard, El Mansari, & Blier, 2009). He also studies this synthetic triple reuptake inhibitor's effect upon monoaminergic lesions (Guiard, El Mansari, Merali et al, 2008). He is building a foundation of

evidence base for future human clinical trial, one research study at a time.

Other research study found results supporting "Vulnerability to cocaine relapse involves neuroadaptation of glutamatergic synapses within the brain's reward system." (Miguens, Botreau, Olias, et al, 2011, p. 623). This animal study may be useful to the development of future research design involving pharmacokinetic and pharmacological manipulations which may modify accumbal glutamate to reduce cocaine seeking drive. Prior research concluded "genetic background may differentially alter the glutamatergic and GABAergic transmission associated with vulnerability to cocaine relapse in the NAcc, and underline the importance of considering individual genetic differences when designing anti-relapse pharmacotherapies targeting amino acid systems" (Miguens, Botreau, Olias, et al, 2011, p. 630).

The same year, the Kenneth Blum team of research associates developed similar research design exploration of the Meso-Limbic system, in human populations who might benefit from amino-acid therapy. "Hypothesizing synergy between acupuncture / aurioculotherapy and natural activation of mesolimbic dopaminergic pathways" they tested the application of putatuve natural treatment modalities for the reduction of drug hunger and relapse" (Blum, Braverman Carbajal et al, 2011, p. 1) with successful result. This protocol has not only been researched, and replicated. It has been patented, manufactured, marketed and brought to market.

Humanity owes a debt of gratitude to pioneering research scientists for their patience, and endurance, in creating animal study research design which contributes to future development of human intervention protocol. The Neurogenetic Research Foundation for RDS have presented publication of new RDS theory, backed by its substantial and growing evidence base in support. There is therapeutic value in the RDS model (Diana, 2011).
Research of RDS solutions (RDSS) is presenting viable alternatives to traditional modalities, which increase therapeutic response options. Potential neurological intervention, gleaned from pharmacological and pharmacokinetic research study of the molecular and cellular processes of relapse, will hopefully revolutionize treatment protocol. . The sciences of RDS and new science exploring neurological processes of craving, drug seeking and relapse are changing the landscape of recovery.

Accomplishing the ultimate goals of stopping the generational cycle of addiction, and resetting neurological imbalances of RDS remain unrealized. As focus shifts in search of population which experience significantly higher risk and/or complexity of addictive expression, we note that gender and/or ethnic variances are minimal. Research of African American variance was

insignificant (Levran, Randes, Correa da Rosa, et al, 2015).

Lets focus upon what matters, rather than what others demand of us. We find extreme variance with populations dually diagnosed with mental illness and co-occurring SUD, as well as significant variance in those populations of survivors who endured adverse childhood experiences such as physical, emotional and/or sexual abuse. In fact Posttraumatic Stress Disorder predicts development of addictive behavioral patterns (Wilsnack, Vogeltanz, Klassen, et al, 1977). Compassion demands that these populations be given research priority. Excluding these populations from research study distorts perspective (Moberg, & Humphreys, 2016) which may result in negating the validity of our diagnostic criteria (Reiger, Laelber, Rae et al, 1998).

The population of individuals inheriting a deficiency of DRD2 Receptors and/or the DRD2 A1 Allele have significantly higher risk for development of impulsive, compulsive and addictive behavioral patterns. Populations with polymorphic influence of the GABRA2 gene display a higher risk of addictive potential. Rather than look across boundaries of gender, or ethnicity, lets look for genetic predisposition. This is the population upon which to focus attention.

If the family is to survive the devastation of RDS (Please note that I purposely did not say addiction because of the negativity and harmful preconceptions with which society has victimized its sufferers), it needs to be informed. Genetic screening is a must. RDS has many manifestations, contributing to a spectrum of dopaminergic disorders beyond impulsive, compulsive, and addictive expression, including depression, Autism, Asberger, Alzheimer, and Parkinson's disease. These are the many faces of RDS. Genetic Addiction Risk Scores (GARS) and possibly outcomes such as asperger can be identified.

Perhaps in commitment to manifesting a brighter healthier future, we turn our focus from disease to wellness, develop more accurate diagnostic criteria, better measurements of wellbeing self-efficacy (McKiernan, Cloud, Patterson, et al, 2011), and abandon ourselves to practice of positive psychological applications from existential, transpersonal and integral perspectives of whole-ism and oneness. "Integrating the science of addiction and the science of well-being" (Gilley, 2017) will empower recovery. We, are responsible for manifesting and "Creating Addiction" (Gilley, 2012). WE can recreate wholeness, wellness, thriving. First LET US thoroughly dismantle false hurtful constructs which disempower rather than heal, expose half truths for the lie they are, and claim powerfulness, rather than powerlessness.

In an ideal world, future research design will align with quantum physics, rather than the reductionist, separatist, Newtonian tendency. Future research will hopefully study energy signals which are one hundred times more powerful than molecular signals. Future research will explore the healing potential of bio and psycho-electro-magnetic frequencies (Gilley, 2016), include exploration of infrared spectroscopy to identify of recovery markers (Dempsey, Harris, Shumway et al, 2015) and effect of frequency unbalance in energy signaling (Balconi, Finocchiaro & Canavesio, 2014). Hopefully future research will focus more upon developing benefit of healing frequency, rather than investing in the weapon-i-zation of frequency. Undoubtedly, the future of RDS and addiction research will provide accuracy of perception, righting a wrong created by hurtful, ugly response patterns of improper addiction perspectives of the past century. Perception determines behavior, on the level of receptor and effector proteins and on the level of the collective population. Yes, just as the quantum field determines the expression of the particle, perception determines behavior. Allow me to set the proper tone. WE are not victims of our heredity. Even epigenetic change is based upon perspective. Cellular intelligence is powerful enough to change genetic heritage. Imagine the power of the collective, aligned with higher truth. Imagine the possibilities. Dare to thrive!

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