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A PROPOSED TREATMENT PLAN MODEL FOR REWARD DEFICIENCY SYNDROME: TO HELP IN RESTRUCTURING THE ADDICTION RECOVERY INDUSTRY

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INTRODUCTION DISCUSSION OF NEUROGENETIC AND EPIGENETIC RESEARCH ADVANCEMENT IN ADDICTION MEDICINE

Approximately 50 years of research have led to new understanding and a new phenotype for impulsive, addictive and compulsive behavioral expression with the successful evidence based concept of Reward Deficiency Syndrome (Blum, Braverman, Holder, Lubar, Miller, Monastro, Commings et al, 2000) which is linking all addictions under a common rubric (Blum, Febo, McLaughin, Cronje, Han et al, 2014), and changing the recovery landscape. Although Kenneth Blum is accredited with first coining the phrase in 1995 (Febo, Blum, Badgaiyan, Baron, Thanos, Colon-Perez, et al, 2017), literally thousands of research scientists have contributed to the advancement of the field of the neurogenetics of addiction (Ducci & Goldman, 2012). There is no debate on the doctoral and post-doctoral levels of neuroscience. Some are informed. Others are not. The evolution of addiction science has revealed a new phenotype. "RDS is the disease, [and] addiction it's symptom" (Gilley, 2018, p. 161; Smith. 2012).

Polymorphic variance can be determined with genetic screening. Although Blum and his associates were not the first to develop genetic screening, they have patented a gene panel map which can predict future RDS behaviors. The test screens for the most researched polymorphic variances: Dopamine 1-4 receptor genes (DRD1, DRD2, DRD3, DRD4), Dopamine Transporter gene (DAT1), Serotonin 2a receptor (5-HTT2a) and the Serotonin Transport gene (5HTTLPR), Mu-opiate receptor (MOR), GABA– B2 Receptor, Mono-Amine-Oxydase A gene (MOA), Calecholamine-Methyl-Transferase gene (COMT) and the PENK Cytochrome P450 gene (Blum, Badgaiyan, Agan, Frantantonio, Simpatico, Febo et al, 2015; Blum, Oscar-Berman, Demetrovics, Barh, & Gold, 2014). Blum acknowledges that over time, they will expand the test to include additional variances which become associated with addiction risk as the scientific evidence base provides support (Blum & Badgaiyan, 2017).

As we enter this Genomic and Neuroscience Era of Addiction Medicine (Blum, & Badgaiyan, 2017; Snow & Lu, 2012), there is molecular neurogenetic evidence for predisposition to Reward Deficiency Syndrome (RDS) (Blum, Modestino, Gondre-Lewis, Chapman, Neary, et al, 2017), which can manifest in impulsive, addictive, compulsive behaviors, as well as contributing to ADHD (Gilley, 2018), depression, Parkinson's and the Autism Spectrum.

Genetic screening allows the exact phenotype subcategory to be identified, with it's unique treatment protocol. Polymorphic variances provide insight for advanced treatment modalities, in the design of treatment for dopamine deficiency, and dopaminergic pathway imbalances (Blum, Thanos, Oscar-Berman, Febo, Baron, Badgaiyan et al 2015) which can result in Anhedonia and Dysphoria (Gold, Blum, Febo, & Badgaiyan, 2018). Genetic screening is both preventive and proactive. It is imperative for identifying and targeting those with genetic proclivity in order to stop the cycle in the next generation (Kendler, Sundquist, Ohlsson, Plamer, Maes, Windleby et al, 2012).

Dr. Kenneth Blum, Dr. John Giordano, and associates have created natural neutra-ceuticals, categorized under the Reward Deficiency System Solutions (RDSS) umbrella, which help to heal the brain (Blum, Febo, Modesto, Gondre-Lewis, Chapman, Neary et al, 2017). This is a natural nutritional treatment modality which feeds the brain the amino acid building blocks for brain repair (Blum, Braverman, Carbajal, Downs, Downs, Giordano et al, 2011).

Dr. Blum recommends dopamine agonist therapy (Blum, Chen, Oscar-Berman, Chen, Lubar, et al, 2011) as the new preferred modality, rather than dopamine antagonist therapy (Blum, Febo, Thanos, Baron, Fratantonio, & Gold, 2015), which has previously been the accepted NIH response model. In addition to advising the activation of dopamine, rather than the blocking, Blum and his associates are researching natural pro-dopamine regulators, nutrigenomics which support healing of the dopaminergic pathway (Blum, Braverman, Dushaj et al, 2018; Blum, Febo, Fried, Baron, Braverman, Dushaj et al, 2017; Blum, Simpatico, Badgaiyan, Demetrovics, Frantantonio, et al, 2015; Blum, Oscar-Berman, Giordano, Downs, Simpatico, Han et al, 2012). The most recent variant KB220Z has produced results which support its effectiveness in activating dopaminergic pathways (Blum, Febo, Braverman, Perez, Colon-Perez, et al, 2015).

Dr. Blum and his esteemed team of associates are now looking into other neurotransmitter pathways and "hypothesize balancing endorphinergic and glutaminergic systems to treat and prevent relapse to reward deficiency behaviors: coupling D-Phenylalanine and N-Acetyl-L-Cysteine (NAC) as a novel therapeutic modality" (Blum, Febo, Fahlke, Archer, Breggren et al, 2015, p. 8). He has begun testing his pro-dopamine regulator as a healing facilitator of normal resting state frequencies for brains which have abnormal EEG frequencies from neuroadaptation and/or RDS (Blum, Chen, Morse, Giordano, Chen et al, 2010). His team has also created new regulation and verification protocol of treatment compliance with the technique they call "Precision Addiction Management (PAM) to combat the Global Opioid Crisis" (Blum, Modestino, Neary, Gondre-Lewis, Siwicki, et al, 2018).

Research has gifted the scientific community with an understanding of how neurological processes contribute to addiction (Willuhn, Burgeno, Groblewski & Phillips, 2014), increase the likelihood of craving (Loweth, Scheyer, Milovanovic, LaCrosse, Flores-Barrera & Werner, 2014) and drug seeking reinstatement (Schank, King, Cheng, Rice, Heilig, Weinshenker, 2014). Research has revealed that in the case of cocaine addiction, abstinence actually increases the likelihood of relapse (Smith, Beveridge, Nader & Porrino, 2016; Miguens, Botreaum, Olias, Del Olmo, Coria, Higuerea-Maltas et al, 2011).

As significant as genes are in contributing influence to the development of disease, they alone do not cause disease. But rather it is the interaction of genetic and epigenetic influences which contribute to outcome. Both heredity and environment contribute causal influence. Environmental components may mean everything that is not genetic or inherited, including but not limited to life experience, trauma, energetic signals of thought and emotion, the opinions and expectations of others, the collective universal conscious, or even the PH or Electro-Magnetic frequency of the intercellular water in which our body's 100 trillion cells reside.

With these exciting new perspectives, science has responded to the challenge of creating new research areas, researching relapse as initiated with cue induced firing of action potential, molecular and cellular influences on relapse; and pharmacogenomics, which is the study of epigenetic response to genetic variance. Hopefully pharmaceutical intervention for epigenetic processes which seem to lock in addictive proclivity, even passing it down to future generations (McRae, Powell, Henders, Bowdler, Hemani, Shah et al, 2014), will be available in the future.

More specifically epigenetics is the study of how environmental influence effects the RNA transcription of DNA, and the way the gene is expressed, through adaptive responses of chromatic, histone and/or methylation processes (NIDA, 2016). Epigenetic factors have the ability to recode and even alter DNA expression, which can be passed down to future generations (Nestler, 2013; Renthal, & Nestler, 2008). Cadet defines epigenetics as "heritable transcriptional changes that are not the result of modified DNA sequences" (Cadet, McCoy, & Jayanthi, 2015, p. 502). Maze and Nestler concur (Maze & Nestler, 2011). Bannon bridged the gap between the neurogenetic and epigenetic interactive influences of Reward Deficiency Syndrome and Substance Use Disorder by providing a "molecular profile of cocaine abuse [which] includes the differential expression of genes that regulate transcription, chromatin and dopamine cell phenotype" (Bannon, Johnson, Michelbaugh, Hartley, Halter, David et al, 2014).

Epigenetics is also changing the landscape of addiction recovery (Maze & Nestler, 2011). Contributions from the Medical University of South Carolina clarify some aspects of addiction and relapse according to epigenetic mechanisms which complicate the issues (MUSC, 2017) Research of "HDAC5, the suppressor gene, did not prevent addiction-like behaviors from forming, but it did prevent later drug seeking and relapse during abstinence – at least in rodents" (MUSA, online, Science Daily, September 27, 2017, p. 2).

Research Science is also exploring genetic and epigenetic interactions of psychiatric disorders, revealing that psychopathology has common genetic components across the board (Klengel & Binder, 2015) and specifically the role of DNA methylation in stress related psychiatric disorders (Klengel, Pape, Binder, & Mehyta, 2014). Enoch was an early contributor to the evidence base for the "influence of gene-environment interactions on the development of alcoholism and drug dependence" (Enoch, 2012, p. 17); early life stressors, such as trauma and abuse, as predictors of future dependence (Enoch, 2011); and the role of GABRA2 in trauma, PTSD and

future addictive behavioral expression (Enoch, 2010; Comings, Muhleman, & Gysin, 1996).

Gene silencing techniques (Bonoiu, Mahajan, Ding, Roy, Yong, & Kumar, 2009) for polymorphic variances have been proven to increase addictive predisposition. Some day in the future "epigenetic variation in specific genes may be used as biomarkers for substance exposure, addiction risk and response to treatment (Cecil, & Viding, 2016, p. 290). Future research will hopefully explore "transcriptional inducibility of gene targets after drug cue re-exposure" (Maze & Nestler, 2011, p. 110). Pharmacogenetic therapy may be available in the next decade to help cocaine and stimulant addiction (Haile, Kosten, & Kosten, 2009). Addiction vaccines are in the research and development stage (Chi, 2011). And hopefully Ibogaine detoxification and Noribogaine therapies (Mash, Ameer, Prou, Howes, & Maillet, 2016; Mash, Duque, Page & Allen-Ferdinand, 2018) will soon be available in the United States as they are in other countries.

BRINGING REWARD DEFICIENCY TREATMENT APPLICATIONS TO THE PUBLIC

A Reward Deficiency Syndrome treatment plan model is presented based upon evidence-based Reward Deficiency System Solutions. In order to address comorbid multifaceted dimensions of illness which manifest in many realms of human experience, the physiological/biological, psychological, social, spiritual and perhaps even the existential, integral treatment of the whole is required.

Expert Dr. John Giordano cautions that causal influences of addiction are not simple, and states that there are many contributing influences which need to be addressed, which are too often overlooked. These include other bio-medical conditions such as: 1) heavy metal toxicity which causes neurological dysfunction and effects neural communications, imitating ADHD and Bipolar symptomology; 2) hyperglycemia, especially in alcoholics, 3) low testosterone in males, 4) decreased thyroid functioning; and 5) symptoms of "high jacked or broken brain" which relates to damage from drug use (Potenza, 2013). Considered the second brain, the gut must also be evaluated, for functional proficiency in regards to digestion, absorption, and the creation of neurotransmitters.

Each patient has his or her own unique contributing and/or causal influences, so a comprehensive treatment plan is required, above and beyond what is considered the Addiction Recovery industry standard. Hopefully, future treatment modalities will include the creation of a unified team of specialists from many interrelated fields, who work together to assist the recovery process (Baron, Blum, Chem, Gold, & Badgaiyan, 2018; CASA Columbia, 2012). Adaptive treatment response is the natural progression of scientific advancement. The following RDS treatment protocol is offered for consideration for inclusion into addiction recovery treatment plans as the industry adjusts to the prevailing RDS model, the new phenotype of addiction.

RDS TREATMENT PLAN

A. Provide information to the client about Reward Deficiency Syndrome (Punzi, 2016) and its many symptomatic manifestations, impulsive, addictive and compulsive behavioral expressions, also including depression, ADHD (Gilley, 2018), Parkinson's and the continuum of degrees on the Autism Spectrum.
B. GARS, Genetic Screening for RDS behavioral expression and Addiction Risk Scores (Blum et al, 2014) reveal genetic variances which will establish the client's phenotype subcategory, with its unique treatment protocol (Modesto, Blum, Oscar-Berman, Gold, Duane, et al, 2015; Blum et al, 2011).
C. Multifaceted brain imaging to assess damage, and identify targets for intervention.
D. Begin nutraceutical regime for brain repair (Blum et al 2012, 2011).
E. Begin pro-dopamine regulator therapy for potential dopaminergic pathway activation (Blum et al, 2017).
F. Evaluate the appropriateness of dopamine agonist therapy (Blum et al, 2015, 2008).
G. Comply with all Precision Addiction Management (PAM) protocol (Blum, Modestino, Neary, Gondre-Lewis, Siwicki, Moran, et al, 2018; Blum, Han, Femino, Smith, Saunder, et al, 2014).
H. Focus upon natural means of achieving dopamine homeostasis, through mindfulness, nutrition, exercise (Archer, Badgaiyan, & Blum, 2017) and music.
I. Introduce neurotherapies such as neurofeedback to balance brain frequencies and offset EEG imbalances (Blum et al, 2010).
J. Mindfulness meditations for spiritual development and relapse prevention skill development (Khusid & Vyrhilingam, 2016; Schoenthaler, Blum, Braverman, Giordano, Thompson, et al, 2015; Witkiewitz, Bowen, Harrop, Douglas, Enkema, & Sedgewick, 2014; Marchland, 2013).
K. Participate in recovery management and enhancement plan development. Attend Twelve Step meetings for support and to create new neural pathways through brain plasticity (Borsten, & Winchell, 2017; Blum, Thompson, Demetrovics, Femino & Giordano, 2015).
L. RDS family education and therapy (Levey, Le-Niculescu, Frank, Ayalew, Jain, Kirlin, et al, 2014).
M. At 30-60-90 days, reassess through neural imaging techniques and self-report to gage progress and degree of neurological regeneration.
N. If necessary, pharmacogenomic and/or pharmacological interventions can be implemented to boost balancing of dopaminergic pathways.
O. Exploration of epigenetic variance may be explored to understand the complexity of induced adaptations.

P. Psychotherapy for pathology and integrative practices for life enhancement (Gilley, 2017; Moliver, Mika, Chartrand, Haussman & Khalsa, 2013).
Q. If comorbid disorders are present and/or persist, address each with psychological and psychiatric perspectives, and develop treatment plan protocol for comorbid mental illnesses, according to the DMS-5 (APA, 2013).
R. Long term continuing quality care for recovery management (Giordano, 2018).

IN SUMMARY

Cutting edge neurogenetic and epigenetic research has provided new insight into RDS causal influence which manifests in impulsive, addictive and compulsive behavioral patterns. Reward Deficiency Syndrome is now understood to be the disease, and addiction a symptom (Gilley, 2018). The need for Reward Deficiency System treatment solutions presents both opportunity and challenge to psychiatry, psychology and the addiction recovery treatment industry. In this era of opioid epidemic (Miller, Miller, Blum, Badgaiyan, & Febo, 2015), providing evidence-based treatment to activate the dopaminergic pathway is crucial if lasting recovery is to be achieved and maintained (Willuhm, Burgeno, Groblewski, & Phillips, 2014). Practitioners and treatment plan modalities will align with cutting edge evidenced based science and its applications to enhance the effectiveness of modern addiction medicine, (Gilley, 2017a; 2017b) in light of Reward Deficiency Syndrome and Reward Deficiency System Solutions research (Gilley, 2018; Snow & Lu, 2012).

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