

Have We Hatched the Addiction Egg: Reward Deficiency Syndrome Solution System™

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Abstract

This article co-authored by a number of scientists, ASAM physicians, clinicians, treatment center owners, geneticists, neurobiologists, psychologists, social workers, criminologists, nurses, nutritionist, and students, is dedicated to all the people who have lost loved ones in substance-abuse and “reward deficiency syndrome” related tragedies. Why are we failing at reducing the incidence of ‘Bad Behaviors’? Are we aiming at the wrong treatment targets for behavioral disorders? We are proposing a paradigm shift and calling it “*Reward Deficiency Solution System*” providing evidence for its adoption.

Keywords: Reward Deficiency Syndrome (RDS) dopamine; Standard of Care; Addiction

Introduction

An accurate diagnosis is required to effectively treat any disorder. This has been recently underscored on the heels of the publication of DSM-V and challenged by the NIMH (http://www.behavioral.net/blogs/tom-doub/rethinking-psychiatric-diagnosis-eve-dsm-5-new-paradigm_nimh?WA_MAILINGLEVEL_CODE=&spMailingID=41480798&spUserID=NTA3NTQ4NTY0MDkS1&spJobID=187662932&spReportId=MTg3NjYyOTMyS0). To diagnose a disorder, the health practitioner must be able to correctly identify, define and classify the dysfunction by either the cause (etiology), mechanism of the cause (pathogenesis), the symptoms exhibited, and/or according to the organs involved. Organ classification can be complicated since many diseases affect more than one organ. This identity classification is necessary to provide a named diagnosis, assign an insurance code for reimbursement, and prescribe the proper drugs (compliance with ‘Standard of Care’). However, a result of this system is that someone with ADHD, Tics or Autism has no tangible relationship to a sex addict, a pathological gambler, or an obese individual. Is there such a connection you might ask? The answer will reveal a whole new paradigm.

In 1990, our laboratory, published their discovery of the “reward gene” (the dopamine D2 Receptor TaqI A1 allele [DRD2 A1]) in the Journal of the American Medical Association (JAMA) [1]. At the time, this gene was called the ‘addiction gene’ and the ‘alcoholism gene’. It turns out that it is the “Reward Gene” as stated in the original paper. The publication of this discovery shook the very foundation of the conventional addiction treatment field and was initially met with intense criticisms and resistance that have diminished over the years. After thousands of confirming studies and published papers over the next 21 years, on August 15, 2011, the American Society of Addiction Medicine (ASAM), the authoritative US society of physicians specializing in addictions, published its new ‘revolutionary’ definition of addiction. In their public policy statement, they cite that,

“Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry.” This means that addiction is a brain disorder not caused by any other life challenges or disorders. They also state that “Genetic factors account for about half of the likelihood that an individual will develop addiction. Environmental factors interact with the person’s biology and affect the extent to which genetic factors exert their influence.” (This is Epigenetics.) In addition, they state, “Addiction affects neurotransmission and interactions within reward structures of the brain.”

Emphatically this new definition of addiction does not diminish the essential role of psychological, spiritual, and fellowship program support in helping addicted individuals reprogram their mental approach to life’s challenges with the positive mental attitudes and habits that enhance the quality of life and strengthen their journey of recovery. This new definition recognizes and adds another extremely important tool to achieve what was previously nearly impossible without it. And, the scientific evidence supporting its success is convincing beyond any doubt.

The first question that jumps to mind is WHY would this preeminent authoritative society on addictions change the definition of addiction? It is because the success rate of the vast majority of addiction

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treatment programs is overwhelmingly abysmal! According to some reports, the relapse rate can be greater than 90% within the first year. The average overall relapse rate of drug addiction is between 40 – 60%, similar to other chronic diseases like Diabetes (Figure 1) [2]. While relapse statistics can vary between 40% to more than 90% within 1 to 4 years, depending on the source, according to ASAM something very important was being overlooked with the conventional approach and required a major paradigm change.

This new perspective is most important as it effects a major change in the approach to treating addictions and all ‘Reward Deficiency Syndrome’ (RDS) behaviors [3]. The term “Reward Deficiency Syndrome” was first coined by one of us (KB) in 1995, and is now defined by the Microsoft Dictionary as “A brain reward genetic dissatisfaction or impairment that results in aberrant pleasure seeking behavior that includes drugs, excessive food, sex, gaming/gambling and other behaviors.” The other behaviors not delineated span an array of disorders, some of which are noted in the table below, and include ADHD, Tics, Tourette Syndrome, autism (incl. Asperger Syndrome), OCD, perverted sexual practices, obesity, and so on. The relationships of these disorders are not clearly apparent without an understanding of the common genetic factors underlying them; this is the connection between these disorders. This leaves conventional treatments to be based on the existing classification system alone, which appears to be woefully inadequate. A new approach is critically needed. This fact could not be more apparent when considering the aberrant behavioral profiles of gunmen involved in school shootings, especially in light of the recent horrible tragedy in Newtown, CT that has irrevocably shattered so many lives. Without the awareness and understanding of how to more effectively influence the gene expression of carriers of genetic variants, the medical establishment is left with the only option of continually medicating these individuals while they undergo various talk therapy and support programs, which doesn’t seem to be effective in preventing these tragic cases.

The stunning impact of ASAM’s new definition was also reported in the autumn 2011 Quarterly Newsletter of the International

Schizophrenia Foundation. They state that “ASAM’s new “Definition of Addiction” knocks the psychological element off center stage, redefining addiction as neurological disorder and an imbalance in the brain’s “reward” circuitry”, also correctly referred to as ‘Reward Deficiency Syndrome’ (RDS). David Smith, MD, founder and past president of ASAM, recently published an article that confirmed addiction as a primary chronic disease involving brain reward that can lead to relapse and fatality if not treated. This scholarly report links all behavioral addictions to common neurochemical mechanism. In fact, Dr. Smith cited Reward Deficiency Syndrome (RDS) as the basis of a broader definition of addiction involving both genetic and environmental factors [4].

The brain reward circuitry includes neurotransmitters involved in ‘feeling good’ that are produced by the brain reward cascade (BRC), which proceeds from serotonin to enkephalins (including endorphins), opiate receptors, GABA, and culminates with *dopamine*; the ‘pot of gold’ payoff at the end of the ‘reward’ rainbow. When levels of these “feel good” chemicals are low or blocked from the brain’s receptors, stress, pain, discomfort, intolerance, agitation and excessive reward deficiencies cause increased cravings and/or a desire for satisfaction from aberrant reward-seeking behaviors (RDS) up to an including pathological violence. So, essentially, addiction went from being solely a ‘software problem’ requiring fellowship and psychological talk therapy programs (i.e. 12 Step, etc.) [5], often including heavy medication, to a hardware problem requiring *nutrigenomic intervention*. Nutrigenomic science studies the influence of nutrition on gene expression and the effect that has on health. Rather than a single (loci) target for a drug via a single mechanism of action by a single ‘active ingredient’ molecule (‘Reductionist’ paradigm), nutrigenomic intervention is a ‘systems neurobiology’ approach and can promote balanced brain chemistry and healthy gene expression. As most of us know, we can’t change our genes, but, we can change or ‘optimize’ gene expression through messenger RNA with nutrigenomic technology. As indicated in ASAM’s definition, and discovered by Blum et al. [1], there are genetic and physiological reasons (as opposed to solely psychological) for excessive cravings, impulses, compulsions, obsessions, addictions, and resulting unhealthy behaviors. Following three decades of research, this was again recently confirmed when scientists at Harvard and Mass General Hospital genotyped over 66,000 people and discovered common DNA variants across five psychiatric disorders [6] suggesting that treatment across these disorders should be common.

The DRD2 A1 variant (the ‘reward, survival, and addiction gene’) discovered by Blum et al [1] to associate with all addictive behaviors has been confirmed [5]. However, its prevalence also varies with ethnic backgrounds ranging from 50% to 85% in African Americans, Hispanics, Asians, and Native Americans [7]. Moreover, prevalence of this gene is greatest in individuals with various impulsive, compulsive, obsessive and addictive disorders from alcoholism and thrill seeking behaviors to excessive gambling, internet gaming, and obesity greater than a 70% prevalence. [8] The evidence demonstrates that people who carry this A1 variant have 30% to 40% fewer dopamine D2 receptors, which predisposes them to dopamine resistance and a much higher requirement for dopamine ‘stimulation’ (or a ‘high’) just to feel normal satisfaction [9]. However, this craving for a dopamine fix does NOT resolve the dopamine resistance. In fact, it just makes it worse. Those suffering from RDS are unable to produce an adequate feeling of well-being and consequently often self-medicate with substances or behaviors that help raise the levels of “feel good” chemicals (especially dopamine) in their system--if only temporarily [10]. The self-medication

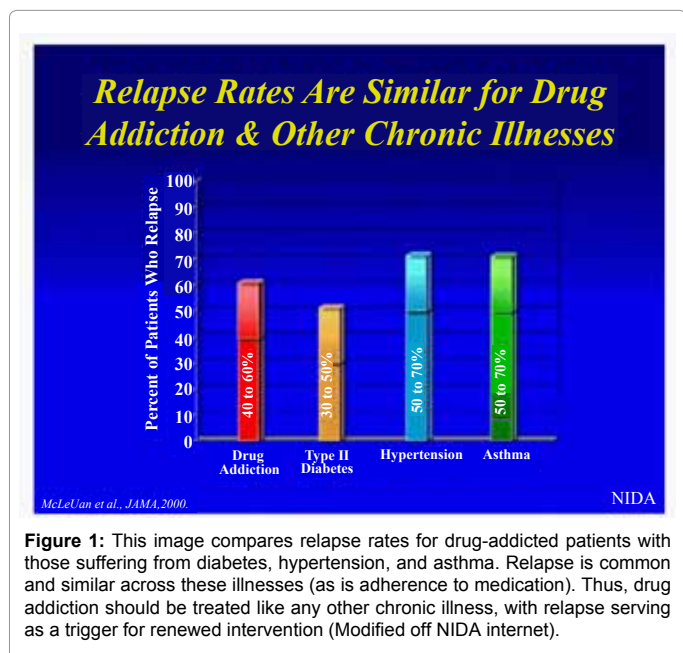


Figure 1: This image compares relapse rates for drug-addicted patients with those suffering from diabetes, hypertension, and asthma. Relapse is common and similar across these illnesses (as is adherence to medication). Thus, drug addiction should be treated like any other chronic illness, with relapse serving as a trigger for renewed intervention (Modified off NIDA internet).

doesn't actually provide the resources that support the manufacture of dopamine, but cause the release of dopamine that can bankrupt or overdraw dopamine stores. However, release of dopamine helps them feel good or gratified for a short while. These substances often include junk foods, sugars, chocolate, alcohol, nicotine or stimulants, but can include a range of excessive thoughts and behaviors. Unfortunately, the temporary relief from self-medicating thoughts and behaviors can bring with it the possibility of more long-term consequences and dangers such as weight gain due to blunted reward circuitry, especially in carriers of the DRD2 A1 form of the gene [11], addictions, health problems, intense remorse, incarceration, death, and inflicting damage on themselves and the lives of family, friends, colleagues, and even 'innocent bystanders'.

In addition, there is the miserable stigma, guilt, regret, and pain in the aftermath. This is also true for over eaters and all types of 'reward deficiency syndrome' behaviors, some of which are noted in the chart below (Table 1).

People with reward deficiencies have difficulty experiencing the satisfying 'reward' that others get from normally pleasurable experiences.

To date, 27 published clinical studies now demonstrate that a patented† KB220Z neuroadaptogen nutraceutical (KB220Z NAAT) complex provides nutritional support for optimal gene expression in the brain reward cascade; to enhance dopamine sensitivity and function, regulate cravings; ease detox, promote weight management*; and enhance focus, concentration, cognition, energy, stress relief, elevated mood, a sense of well-being, and vitality. This is especially important for people who are unable to experience satisfaction from normally rewarding thoughts and behaviors due to genetically predisposed Reward Deficiencies [12].

Over the last 50 years, we have created and explored a number of important tools to diagnose addictions, evaluate compliance to treatment medications, monitor abstinence, and enhance the quality of life of the "recovering" addict. In an effort to understand and optimize the gene expression for all the neurotransmitters involved in the brain reward cascade (serotonin down to dopamine), over the years we investigated the nutrigenomic influence of various nutraceuticals on genes involved in the synthesis, transport, reception, and disposal of those neurotransmitters. As a result, we have (a) developed the Genetic Addiction Risk Score (GARS), a DNA based panel of candidate genes to stratify risk for all reward dependent behaviors, (b) utilized the Comprehensive Analysis of Reported Drugs (CARD™ urine screen) to determine treatment outcomes, and (c) developed the first natural dopamine D2 receptor (D2R) activator to provide enhancement of "dopamine sensitivity" in treatment. Using functional magnetic resonance imaging (fMRI), we have observed brain resting-state abnormalities in heroin-dependent individuals in regions that could negatively impact decision making, inhibitory control, and affective responses. Other studies have reported persistent abnormalities in orbitofrontal cortex following one month of heroin withdrawal. Zijlstra et al. [13] found abnormally lower baseline D2R availability in the left

caudate nucleus in opiate-dependent subjects, and D2R availability in the putamen correlated negatively with years of opiate use. Opiate-dependent subjects also demonstrated higher dopamine release after cue-exposure in the right putamen than controls, and dopamine release was positively correlated with chronic craving and anhedonia (lack of pleasurable reward). Treatment strategies that increase D2Rs would seem to be an obvious and logical approach to prevent relapse in opiate and other addictions.

Utilizing our GARS panel, we found a risk stratification of the 70 genotyped addicted patients to be as follows: 14% Low Risk; 81% Moderate Risk and 5% Severe Risk [14]. Moreover, in unpublished work, utilizing the CARD™, we found compliance to prescribed medications during recovery treatment across the six eastern states to be only 67%, whereas only 39% of these patients were found to be abstinent from misusing drugs of abuse. We also found that whereas 92% of patients in opioid treatment utilizing methadone were compliant, only 49 % of these patients were abstinent. A similar finding was obtained in Suboxone maintenance patients where the compliant percentage was 88%, but only 48% were considered abstinent based on CARD. Surprisingly, in the Suboxone and Methadone groups, we found high opioid misuse. In the fMRI study, we report that one-hour after acute administration of the patented KB220Z NAAT in five heroin addicts, a BOLD activation was observed in caudate-accumbens dopaminergic pathways compared to placebo along with a reduction of the higher dopaminergic activity in the putamen. Moreover, in 10 heroin dependent subjects, we found three brain regions of interest to be significantly activated from resting state ($p < 0.05$) one hour post KB220Z NAAT. Additional work with qEEG in our laboratory revealed in Caucasian abstinent psychostimulant addicts that the KB220Z NAAT, after one hour of oral administration, significantly induced an increase in both alpha and low beta bands in prefrontal cortex and the cingulate gyrus [15,16].

Along with scientists at the University of Florida, College of Medicine in the Department of Psychiatry & McKnight Brain Institute we are embarking on fMRI animal work using variants of the KB220Z NAAT to further identify specifically affected brain regions.

Summary

Based on these studies, we are proposing a new paradigm shift whereby accurate determinations can be made for (1) predisposition risk of Reward Deficiency Syndrome (RDS) by utilizing GARS™, (2) suitability of candidates for a drug treatment protocol, (3) treatment outcome by utilizing CARD™, and (4) dopaminergic activation by utilizing the KB220Z NAAT, and (5) attendance to a self-help program & fellowship. The fMRI results in humans, and possibly in nonhuman animal models, coupled with qEEG studies suggest a putative anti-craving/anti-relapse role by direct or indirect dopaminergic interaction for KB220 variants. We are getting closer to actually "hatching the addiction egg"!

Addictive Behaviors	Impulsive Behaviors	Obsessive & Compulsive Behaviors	Personality Disorders
Severe Alcoholism	Attention-Deficit Disorder Hyperactivity	Aberrant Sexual Behavior	Conduct Disorder
Polysubstance Abuse	Tics & Tourette Syndrome	Internet Gaming and Obsessive Texting	Antisocial Personality
Smoking	Autism (including Asperger Syndrome)	Pathological Gambling	Aggressive Behavior
Over Eating – obesity		Workaholism & Shopaholism	Pathological Cruelty & Violence

Table 1: Illustrates a number of Reward Deficiency Syndrome (RDS) behaviors [5].

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Conflict of Interest

Kenneth Blum, B.W Downs, John Giordano, Roger L Waite, Margaret A Madigan have interest in KB220™ complex. There are no other conflicts of interest and all authors approved the manuscript.

† US Patent 6,132,724, 6,955,873, and EU Patent EPO979092 with other domestic and international patents pending.

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