Editorial

DOI: http://dx.doi.org/10.53043/2347-3894.acam11003

Reward Deficiency Syndrome Solution System (RDSSS) A Genetically Driven Putative Inducer of "Dopamine Homeostasis" as a Futuristic Alternative to Enhance Rehabilitation Instead of Incarceration

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Asian Journal of Complementary and Alternative Medicine. Volume 11 Issue 01

Published on: 11/01/2023

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Cite this article as: Blum K, Green R, Mullen P, Han D, Bowirrat A, et al. *Reward Deficiency Syndrome Solution System (RDSSS) A Genetically Driven Putative Inducer of "Dopamine Homeostasis" as a Futuristic Alternative to Enhance Rehabilitation Instead of Incarceration.* Asian Journal of Complementary and Alternative Medicine, Vol 11(1), 11-14:2023.

Since the seminal discovery reported by Drs Kenneth Blum & Ernest P. Nobles in JAMA 1990 of the association of the DRD2 Taq A1 allele and severe alcoholism, the field of Psychiatric Genetics was born, and the understanding of the relationships between DNA polymorphisms and epigenetic insults exploded [1]. Nature vs. nurture is now thought to be 50/50. Most recently, the criminal justice world was profoundly and excitedly reminded how genetic information could help us understand to some degree why many people knowingly drive while drunk causing havoc and even death while under the influence of alcohol and or drugs or combinations of both [2]. A paper published in the prestigious St. Mary's Law Review edited by Brent Bauer ESQ, authored by Kenneth Blum, PhD, Richard Green BSMA and Paul Mullen, ESQ, demonstrated how genetic testing could help convert incarceration to probation and rehabilitation utilizing the patented Genetic Addiction Risk Severity Test, developed by Dr. Blum and his team of genomic scientists, and used in this context with chronic DWI offenders [2].

According to basic tenets of Western philosophy, individual development is dependent upon the uniquely human ability to exercise free choice. Modern science challenges this proposition, however, by providing support for the development of an individual according to pre-determined genetic characteristics. Anglo-American criminal law bases excuses on "causal theory." When an agent is caused to act by a factor outside his/her control, he/she is excused; in principle only those acts not external factors are inexcusable. This is indeed the first case study to help the criminal justice system untangle "determinism vs. free will" through genetics. Specifically, comparing the genetic argument to something

like the well-known (though often misunderstood) insanity defense is a false equivalency – the argument is not that these offenders are unaware of what they are doing – rather, the argument is that they have a genetic pre-disposition to problem drinking [3]. This is not about excusing behavior. This is about showing that certain types of substance use disorders will not be successfully treated by incarceration. Communities have an interest in keeping chronic drunk drivers off the road, but incarceration is a short-term solution. Treatment – real medically-integrated treatment, based on solid genetic and psychiatric evidence – seeks a permanent solution [4]. In fact, DWI is a serious health, legal, and financial burden to society and the individual. The results of the analyses by Beaver & Barnes [4] suggested that genetic factors explained 53% of the variance in DUIs/ DWIs and the nonshared environment explained 47% of the variance.

A few decades ago, the 1996 laureate of the Nobel Prize in Literature, Wisława Szymborska (Polish Poet), wondered "Where is the place of free will, which manages to be and not to be." We believe that our team has provided an alternative to harsh sentencing because our seminal work is now answering what was then a rhetorical question that has permeated human thought since antiquity. Moreover, the discovery that the genes underlying dopaminergic and related neurotransmitter systems are implicated in DWIs, and other behavioral choices has profound implications for multiple areas, including neuroscience and, more recently, jurisprudence [2].

Thus, to our knowledge, this precedent is a pivotal legal case utilizing genetic information to advocate rehabilitation for carefully chosen and genetically characterized individuals in the SUD space instead of incarceration. While our work has now been extended to at least 31 other DWI offenders also facing years in prison, some life, with a successful conversion to probation and rehabilitation based on GARS; the team has already saved approximately 220 years in prison.

The Genetic Addiction Risk Severity (GARS) test measures DNA gene polymorphisms that help to identify DNA-induced severe risk for alcohol and psychoactive drug use disorders [5]. It is of particular interest that while major scientific key opinion leaders continue to endorse the use of powerful opioids to treat Opioid Use Disorder" (OUD) our team argues with this uncanny approach in the long-term with increases in opioid induced Fentanyl laced products killing hundreds of thousands annually globally [5].

It is well-known that one's genetic make -up could set up an individual to uncontrollable addictive -like tendencies leading to full-blown, for example, OUD. One important aspect related to the fact that the "no Go" filter in terms of behavior related to the presence of the DRD2 TAQ A1 ***allele*** with a 40% reduction in DRD2 receptors at birth varies across different ethnic groups whereby the America -Indian carriers it at 85%, Asian as 72% and Ashkenazi Jews at 6% [6]. Unfortunately, in the Asian population, they have also an issue with metabolizing alcohol because of the acetyl dehydrogenase problem [7].

In this short editorial we are encouraging the addiction psychiatry field to reconsider the ubiquitous prescribing of Opioids to treat OUD without considering alternative and complementary medical approaches such as utilizing a genetically based novel approach consisting of "Reward Deficiency Syndrome Solution System" whereby the patient is firstly genotyped using the GARS (DRD1-4,DAT1, COMT, MAOA, GABR3, AND 5-HTTLPR) and then based on these results provided with a highly researched customized neutraceutical known as KB220/KB220Z variants shown to have many -anti reward deficit effects [8].

Specifically, we have shown that KB220z induced an enhancement in BOLD activation in caudate-accumbens-dopaminergic pathways compared to placebo following one-hour acute administration. In addition, KB220Z™ also reduced resting state activity in the cerebellum of abstinent heroin addicts. In the second phase of this pilot study of all ten abstinent heroin-dependent subjects, three brain regions of interest (ROIs) significantly resulted in activation from resting state by KB220Z compared to placebo (Figure 1). Enhanced functional connectivity was observed in a putative network that included the dorsal anterior cingulate, medial frontal gyrus, nucleus accumbens, posterior cingulate, occipital cortical areas and cerebellum [9].

It is noteworthy, that in agreement with the research of Blum's group on the role of dopamine in alcohol withdrawal (1976) [10], the Gold & Dackis dopamine depletion hypothesis in cocaine dependence (1985) [11], Wang & Volkow's Pet work on dopamine and obesity (2001) [12] and Thanos's work on gene therapy and DRD2 enhanced expression and resultant reduction of both alcohol and cocaine intake in animals (2204, 2008) [13,14], the work of Demetrovics group work on showing thar dopamine is a "wanting" molecule not "liking" (2022) [15], provides the rationale for futuristic intensive investigation.

In fact, this alternative approach is what Blum's group have utilized with the various individuals that severe sentencing due to unwanted DWIs were converted to probation and rehabilitation instead in a number of cases prison time even life [2]. This seminal work is in progress with now over 31 cases

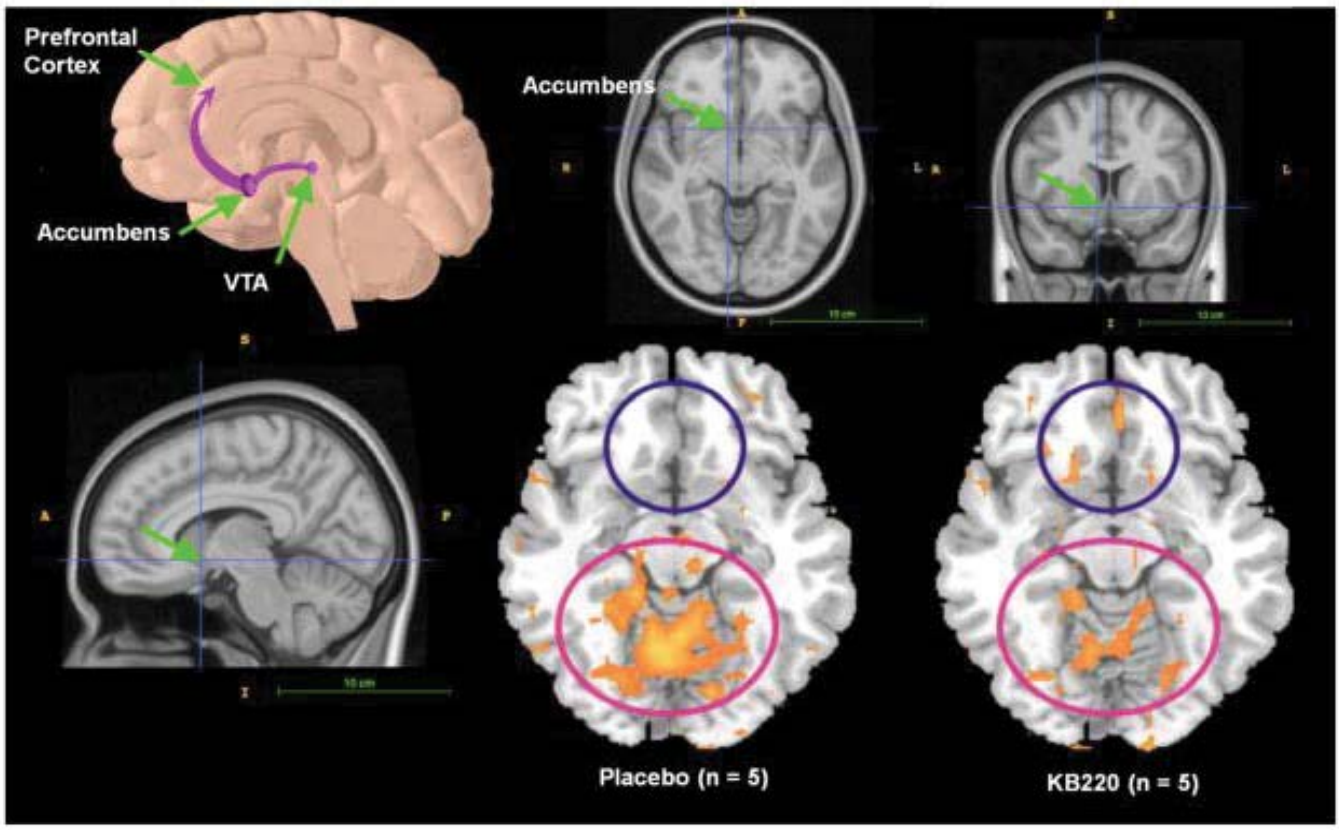

Figure 1: Location of the nucleus accumbens in human CNS.

Resting fMRI Data Analysis in the heroin users (n=5) before and after KB220Z™ and placebo. Standard atlas shows the location of the nucleus accumbens (surrounding area) with significant increases in rsfMRI response with KB220Z. With Permission Blum, et al. [9].

adjudicated and the results will be published elsewhere. With this mind, we believe that futuristic out of the box thinking is tantamount to a better clinical outcome in the long-term as this alternative complementary medical approach be more universally accepted following additional studies [16,17] .

ACKNOWLEDGEMENT

The authors appreciate the expert edits of Margaret A. Madigan.

AUTHOR CONTRIBUTION

KB wrote the initial draft which was commented on and edited by all the co-authors.

CONFLICT OF INTEREST

Dr. Blum is the inventor of GARS and KB220 and there are patents issued and pending which have been assigned to either Synaptamine Inc., or TranspliceGen Holdings LLC.

FUNDING

The article was supported in part by R41 MD012318/MD/NIMHD NIH HHS/United States to KB and Marjorie Gondre-Lewis (Howard University). R.D.B. is the recipient of NIH R01NS073884.

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