Genetics of Reward Deficiency Syndrome (RDS) and SUDs in the Brain

Presented by Lyle R. Fried, CAP, ICADC

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Webinar Presenter

Help For Our Heroes
Transformations
Treatment Center

Webinar Learning Objectives

LO #1
Define Reward Deficiency Syndrome

LO #2
Detail the workings of the neurotransmitters involved in the Brain Reward Cascade (BRC)

LO #3
Detail the holistic interventions that can normalize reward circuitry homeostasis during recovery
• All substance use disorders have a common neurochemical thread which is both genetic (DNA), and epigenetic (environmental influences).
• Dopamine deficiency is the common pathway
• That’s how transfer of drug and non-drug disorders occur.
• Non-drug disorders include behaviors like food, sex and gaming.
• Substance and non-substance disorders are a subsets of RDS.

What is the difference between Reward Deficiency Syndrome (RDS) and SUDs?

• RDS is a relative failure of the dopaminergic system which plays a major part in brain reward mechanisms.
• The syndrome, has been linked to dopaminergic dysfunction; acute excess or chronic deficit of dopamine release in the brain reward circuitry.
• This deficiency includes various condition, (such as substance abuse, smoking, obesity, pathological gambling, attention deficit hyperactivity disorder in which the subject seems to be unusually concerned to achieve reward.
• Polymorphisms (gene variants) of a number of reward genes including serotonin, endocannabinoids, GABA, glutamate and dopamine have all been correlated with chronic dopamine deficiency and reward-seeking behaviors.

REWARD DEFICIENCY SYNDROME (RDS)

"Reward Deficiency Solution System" consisting of the following:
• Genetic Addiction Risk Score GARS
• Comprehensive Analysis of Reported Drugs (CARD)
• Dopamine Agonist Therapy (i.e., KB220z, etc.)
• Pre/post mRNA analysis of gene expression
• Many holistic and psychological additions (yoga, massage, dopamine boosting foods, meditation, trauma therapy, brain spotting, neurofeedback, auriculotherapy, etc.)
• 12 step programs and traditions

To induce "tonic dopamine homeostasis" in recovery
There are over 110,000,000 people in the U.S. alone who have a genetic variant (DRD2 A1) that would put them at risk for addiction.

**REWARD DEFICIENCY SYNDROME within the US POPULATION**

- 67% of the US Population is at risk for Reward Deficiency Syndrome
- 33% are not at risk

- 58% of Hispanics carry the DRD2 A1 gene
- 72% of Asians carry the DRD2 A1 gene
- 85% of Native Americans carry the DRD2 A1 gene

**RDS: A Function of the Reward Genes**

- Addictive substances: Alcohol, Cannabis, Opioids, Sedatives/Hypnotics, Stimulants, Tobacco, Cocaine, Food
- Non-addictive (non-substance): Thrill seeking (Roulette), Sexual Sadism, Sexual Masochism, Hypersexual, Gambling, Internet Gaming
RDS: A Function of the Reward Genes

**IMPULSIVE**
- Spectrum Disorders
  - Attention-deficit hyperactivity (ADHD)
  - Tourette and Tic Syndromes
  - Autism
- Disruptive
  - Conduct
  - Intermittent Explosive
  - Oppositional Defiant
  - Exhibitionistic

**OBSESSIVE COMPULSIVE**
- Body
  - Obsessive
- Sex
  - Excoriation
  - Skin picking
- Non-Sexual
  - Self Injury

**PERSONALITY DISORDER**
- Paranoid
- Schizoid
- Borderline
- Schizotypal
- Histrionic
  - Narcissistic
  - Avoidant
  - Dependent
  - Post Traumatic Stress Disorder (PTSD)
Polling Question #1
Genetic Testing for RDS can provide diagnoses for SUDs
A. True
B. False

One pathway important to understanding the effects of drugs on the brain is called the reward pathway. This reward pathway involves several parts of the brain, some of which are highlighted in this image: the ventral tegmental area (VTA), the nucleus accumbens (NA), and the prefrontal cortex (PFC). When activated by a rewarding stimulus (e.g., food, water, sex), information travels from the VTA to the nucleus accumbens and then up to the prefrontal cortex.

The Limbic System

![Image of the brain highlighting the ventral tegmental area (VTA), the nucleus accumbens (NA), and the prefrontal cortex (PFC)]
A neurotransmitter is a chemical messenger which carries messages between neurons. Dopamine is a neurotransmitter. The interaction of neurotransmitters (like serotonin, cannabinoids, endorphins, GABA and glutamate) cause the net release of dopamine in the reward site of the brain, the Nucleus Accumbens. Stress induces the release of the stress molecule Norepinephrine and dopamine blocks its effects. The release of dopamine also causes feelings of well being, motivation and pleasure.

How does Dopamine get released in the brain to enhance well being, motivation and reduce stress?

The Brain Reward Cascade:

- Unhappy Brain
- Happy Brain
In the absence of neurotransmitters there is NO capacity to feel pleasant feelings.

In the absence of neurotransmitters you experience cravings, anxiety, depression, and more.

Endorphins stop cravings without changing normal thirst...

Stress lowers brain endorphins and increases craving behavior...

Blum et al. PNAS 1983
Polling Question #2
What parts of the brain are affected by SUDs
A. The Prefrontal Cortex (PFC)
B. The Amygdala
C. The Limbic System
D. All of the above

Increasing stress elevates cortisol, adrenaline and other factors. Elevated stress hormones decreases happy, relaxed “chill” neurotransmitters. This leads to additional cravings for dopamine.

Sources of Stress:
- Fear and uncertainty
- Poor sleep
- The death of a loved one
- Divorce
- Loss of a job
- Increase in financial obligations
- Having a heavy workload or too much responsibility
- Attitudes and perceptions
- Getting married/Relationships
- Moving to a new home
- Chronic illness or injury
- Emotional problems (depression, anxiety, grief, guilt, low self-esteem)
- Taking care of an elderly or sick family member
- Traumatic event, such as a natural disaster, theft, rape, or violence against you or a loved one
fMRI of Caudate Region of Brain following Food, Music & Cocaine

Persynaptic DA release above rest

DA Release Pattern in RATS During Sexual Intercourse

Male
Female
Resting DA Level

DA Release (micro dialysis)

Time in Minutes

Neurotransmitter
Receptor
Mitochondria
Wolfs
Synaptic cleft
Axon
Axon
GARS (Genetic Addiction Risk Score)

In 1990 Dr. Kenneth Blum (UT-San Antonio) and Dr. Ernest Noble (UCLA) found the first clear association between a specific gene and addictive behaviors. In that groundbreaking study, a DNA variant of the DRD2 gene was associated very significantly with severe alcoholism. Nearly 30 years and thousands of studies later, the field of psychiatric genetics is now firmly established, and Dr. Blum has developed the first researched-based genetic test called the Genetic Addiction Risk Score (GARS)

The GARS score describes a person’s genetic predisposition to Reward Deficiency Syndrome (RDS). RDS is marked by a reward-seeking, addictive, and compulsive behaviors. Genetic research links certain established DNA variations within genes to these behaviors.
Polling Question #3
Why provide the GARS test to someone we already know has a SUD or RDS behaviors?

A. Combat Denial  
B. Assist with M.A.T. dosing  
C. Guide Nutritional Efforts  
D. Process Guilt  
E. All of the above
Efficacy of Precision Targeted Amino Acid treatments

<table>
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<th></th>
<th>Cocaine</th>
<th>Alcohol</th>
<th>Opioid</th>
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<td>Amino Acid Therapy Rate</td>
<td>80%</td>
<td>70%</td>
<td>100%</td>
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<tr>
<td>Control Relapse Rate</td>
<td>50%</td>
<td>60%</td>
<td>80%</td>
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The amino acid blends have also been studied for hoarding/shopping, PTSD, carb binging, & more.


Neuroimaging Studies – Resting State fMRI After One Dose

This is a scan of the first ever fMRI study in abstinent Chinese heroin addicts after one hour of administering KB220z indicating actual intense activation of the dopamine pathway in the reward site of the brain. The yellow coloration indicates activation. The hyperactivity in another part of the brain involved in emotionality is also reduced significantly following one dose of KB220z. So chronic use will lead to enhanced dopamine activity and as such reduced craving and regulation of the cingulated gyrus as well and reduced relapse.
Treatment Protocols based in Genetics and Neuroscience

As a result of precision DNA directed protocols for neurotransmitter homeostasis & normalized brain waves…
- cravings and withdrawals are decreased
- stress is decreased
- mood is elevated
- decision-making improves

Polling Question #4
What parts of the brain are affected by SUDs
A. The Prefrontal Cortex (PFC)
B. The Amygdala
C. The Limbic System
D. All of the above
Thank You!
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