

Rethinking Dual Disorders

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Nestor Szerman. Faculty Disclosure

<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
Janssen	X	X						
Ferrer	X							
Lundbeck	X	X						
Indivior	X							



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Rethinking Dual Disorders

Outline

- 1- Epidemiological evidence of DDs
- 2- Definition of the Term DDs
- 3- DDs in the field of Mental Disorders
- 4- Conclusions



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1- Epidemiological evidence of Dual Disorders (DDs)

- 1- ECA study
- 2- NCS
- 3- NCS-R
- 4- NESARC
- Dual Disorders are an expectation not an exception.



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Epidemiological evidence of Dual Disorders (DDs)

- **Only 7.4% of these individuals receive treatment for DDs***

- * SAMHSA. 2015. About co-occurring disorders

SAMHSA: SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION

Why is this?



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- **2- Definition of the Term DDs**



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DUAL DISORDERS: “This is the term used in the mental health field to refer to those patients who suffer from an addictive disorder and other mental disorders.

They can occur simultaneously or, even more importantly, sequentially throughout the lifespan” *

(*Szerman and Martinez-Raga, 2015)

which came first?



or



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DUAL Disorders: The Reality

Dual Disorders have been denied for years.



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“DUAL” Disorders

Are we talking about TWO different and separate mental disorders?

Or are they multiple manifestations of a single clinical entity?

*Torrens et al, EMCDDA, 2015;

*Szerman et al, Addiction Disorders & their Treatment, 2013



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Dual disorders?

“The high rate of comorbidity between mental illness and substance abuse is likely to reflect common contributing factors and brain substrates.”

Comorbidity is both a high risk for psychopathology

non. It reflects frequency of psy-

¹VOLKOW. *Am J Psychiatry* 2001; 158: 1181-1183.

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Why is “Comorbidity” problematic?

COMORBIDITY: Describes the relationship between two independent and different categorical diagnoses.

Are DDs (in fact) two independent diagnoses?



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**Dual
Diagnosis**

COMORBIDITY

VS



**Co-Occurring
Disorders**

Dual disorders



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DUAL DISORDERS: The definition

- The **TERM** necessarily specifies a **RELATIONSHIP**, and also implies **INTERACTION** which could reflect common brain factors. (Volkow, 2008; Drake and Green, 2015, Wilkow et al, 2016).
- **Co-occurring disorders** or co-existing disorders describe the same concept as DDs and it is an accepted term in the USA and Canada and can be used interchangeably.
- Meanwhile in the Spanish language the most widespread and accepted term is "**dual pathology**" (Szerman et al, 2013, Morisano et al, 2014).

3- DUAL DISORDERS in the MENTAL HEALTH FIELD

DUAL DISORDERS and
EVOLUTIONARY
PSYCHIATRY

DUAL DISORDERS as
NEURODEVELOPMENTAL
DISORDERS

**THE NIH BRAIN
INITIATIVE (2013)**

DUAL DISORDERS as
GENETIC DISEASES

DUAL DISORDERS and
PRECISION MEDICINE

Addiction: Brain disease*

- ***“Scientific advances in the field of addiction have forever debunked the notion that addiction reflects a character flaw under voluntary control, demonstrating instead that it is a disease of the brain.”***

- * Baler R & Volkow N 2011

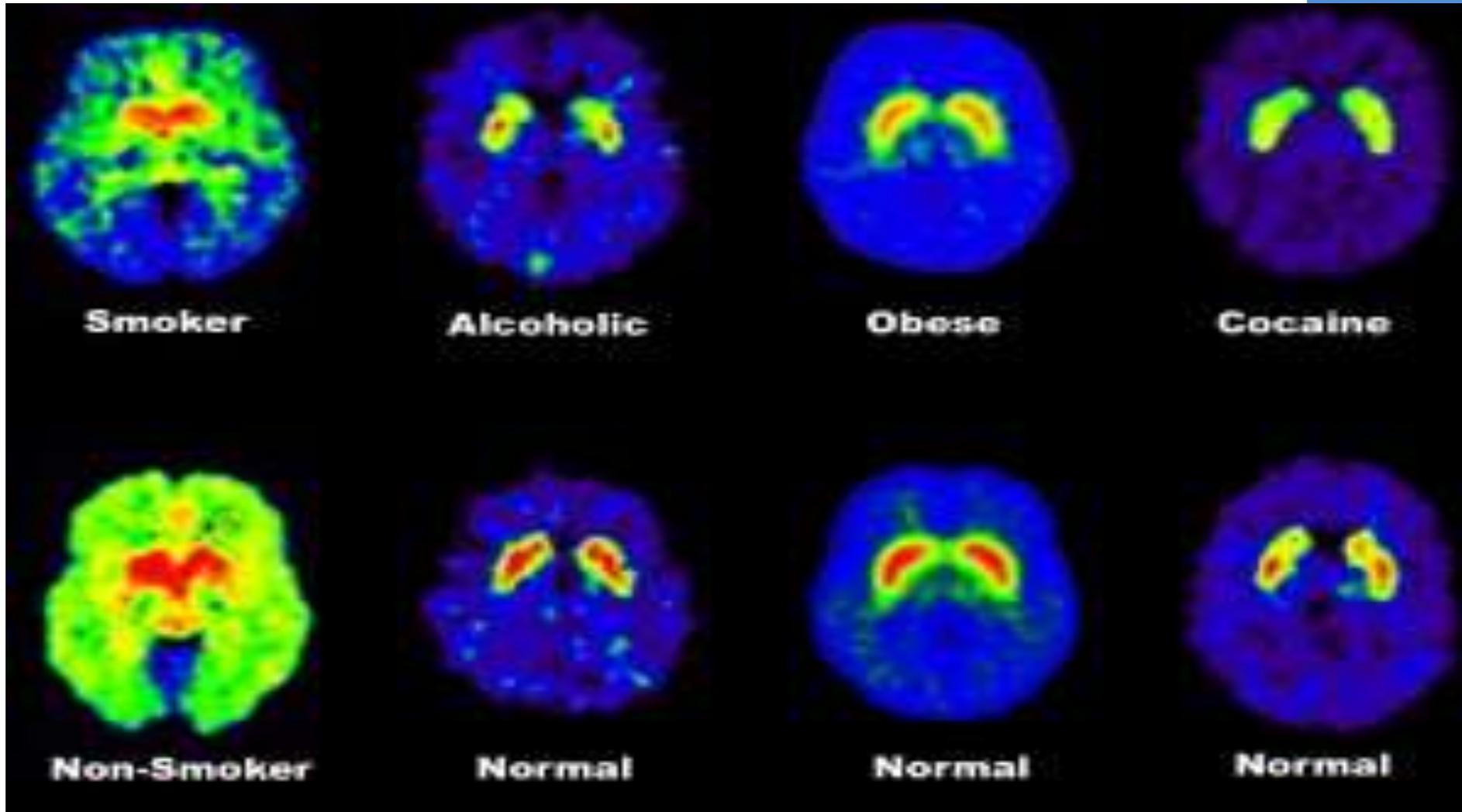


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- Neurobiological evidence of **ADDICTIONS** and DDs



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Neurobiologic Advances from the Brain Disease Model of Addiction

Nora D. Volkow, M.D., George F. Koob, Ph.D., and A. Thomas McLellan, Ph.D.



Neurobiologic Advances from the Brain Disease Model of Addiction*

Only a minority of people who use drugs ultimately become addicted.

In fact, the most severe phenotypic characteristics of addiction will develop in only approximately 10% of persons exposed to addictive drugs .

Why is this?

Susceptibility differs because people differ in their vulnerability to various neurodevelopmental, genetic and environmental factors.

* Volkow ND, Koob GF, McLellan AT. N Engl J Med 2016



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New paradigm on addiction

- Nobody can choose to be addicted.
- Only the individual who has this susceptibility, to being addicted, becomes addicted



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Behavioral Addiction Disorders

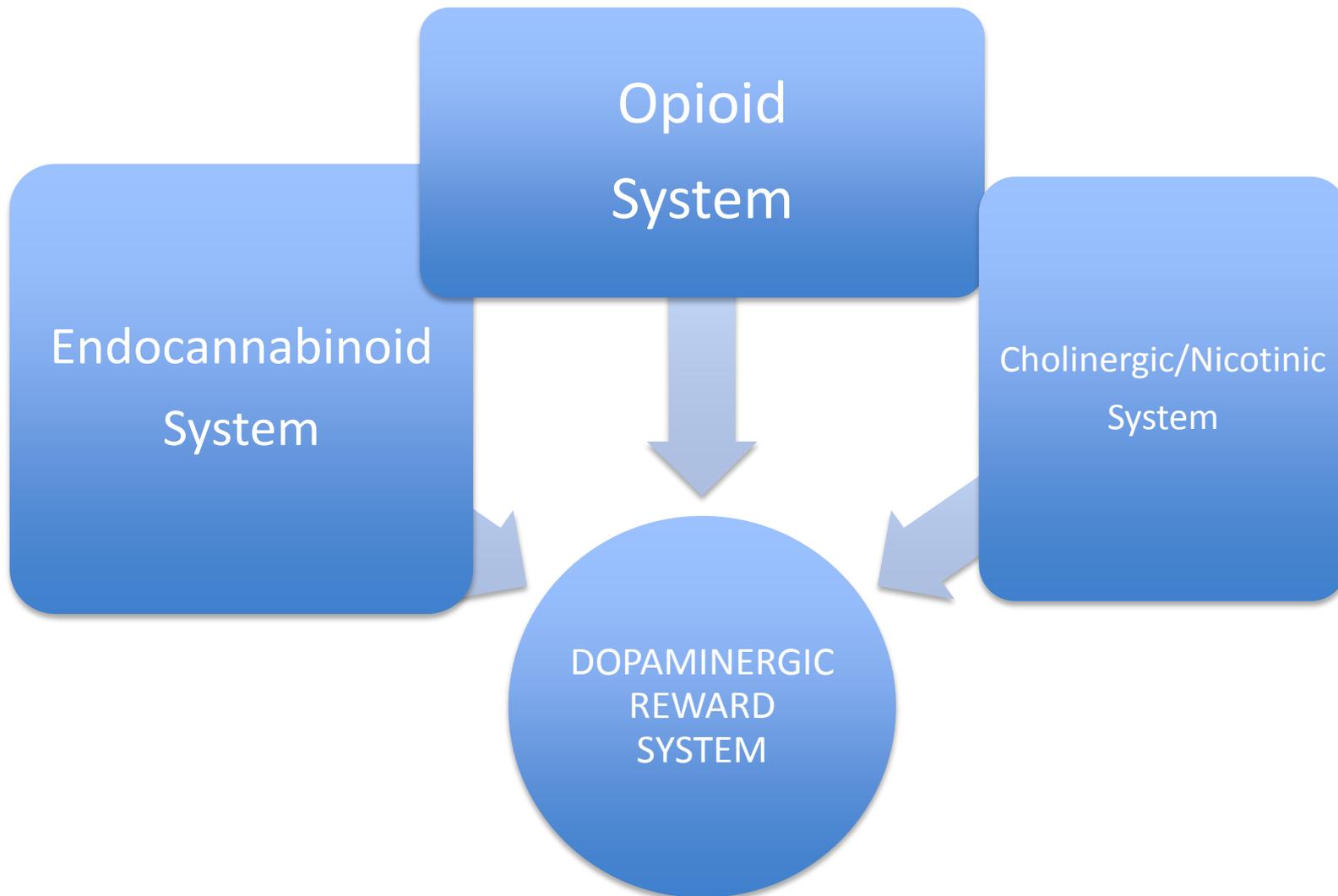
- ***“Current research suggests neurobiological similarities between OBESITY, BINGE EATING DISORDER, GAMBLING USE DISORDER AND SUBSTANCE USE DISORDER.”****

* Van Buskirk KA, Potenza MN. The treatment of obesity and its Co-Occurrence with SUD. J Addict Med 2010; 4 (1)



All psychoactive substances with abuse potential, bind to some endogenous system*

* Szerman et al, ADTT, 2013



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How relevant are these systems?

- From an **evolutionary perspective** they have evolved for individual and evolutionary **survival** of the species, not to “**get high**”.
(Szerman et al., 2013).
- **Both addictive behaviors** and other **mental symptoms** can be explained by an **inherited and/or acquired deficit** in these systems and brain circuits. (Szerman and Peris , 2015).
- In fact these systems and circuits seem to play a **crucial role in all mental disorders**



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“These fundamental biological processes, when disrupted, can alter voluntary behavioral control, not just in drug addiction but also in other related disorders”.

Volkow NR, Koob JF, McLellan Neurobiology advances from the brain disease model of addiction. T. N Engl J Med. 2016, 374; 4: 363-71



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Evolutionary Psychiatry*

Emotions are the result of a long evolutionary process.

Emotional responses exist because they increase our ability to survive.*

Common genetic variants: good genes or bad genes?

Depending on the different context, genetic variants may represent a risk factor or a protective factor.*

The **harmful environment** is a risk factor (i.e. victims of child abuse), although in some individuals the traumatic experience increases their life resilience.*

*San Juan J. Tratar mente o cerebro?. Desclée de Brouwer. 2016

Evolutionary Psychiatry and Dual Disorders

From an **evolutionary perspective**, animals would benefit from a neural mechanism (circuitry) that supports an animal's ability to pursue **natural rewards** (food, water, sex...).

- However these **circuits are sometimes dysfunctional**, leading to various types of disorders.

*Wang GJ, Volkow ND, Fowler JS. Dopamine Deficiency, Eating and Body Weight. In Food and Addiction, editors: Kelly D Brownell and Marc S Gold. Oxford University Press 2012. Chapter 28: 184-193



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Evolutionary perspective Social Anxiety Disorder and Alcohol Use Disorder.*

- **Social Anxiety Disorder** often precedes, **Alcohol Use Disorder**
- **Alcohol exerts effects upon evolutionarily conserved emotion circuits, and can reduce or block anxiety.**
- As such, the use of alcohol can artificially signal the absence or successful **management of social threats.**

* Bullett A, Miloyan B, Brilot B, Gullo MJ, Suddendorf T. J Affect Disord. 2016 Feb 17;196:62-70

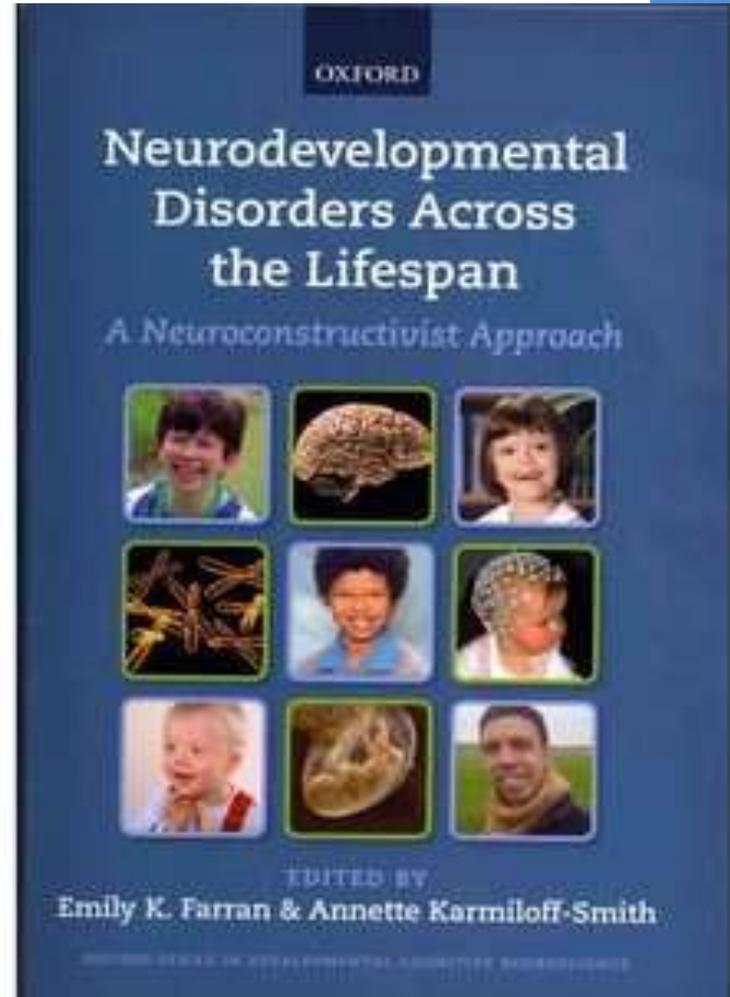


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Neurodevelopmental disorders and DDs.



When do the first symptoms of addiction and DDs start?

A neurodevelopmental model *

- **“Addictions (*and Dual Disorders*) are commonly preceded by “problems” in childhood and adolescence.”**
- For many individuals addiction and DDs begin with the **early expression of psychopathology**

* Leyton M, Vezina P. Dopamine ups and downs in vulnerability to addictions. A neurodevelopmental model. Trends Pharmacol Sci. 2014;35(6):268-76.



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which came first?



or



- From the NEUROSCIENCE perspective, it is known that **the brain presents changes long before MENTAL DISORDERS are diagnosed.**
- These brain changes can occur with sub threshold symptoms, that precede the onset of disease: **substance use disorder or the first psychotic symptom,** **making the egg or chicken debate irrelevant**

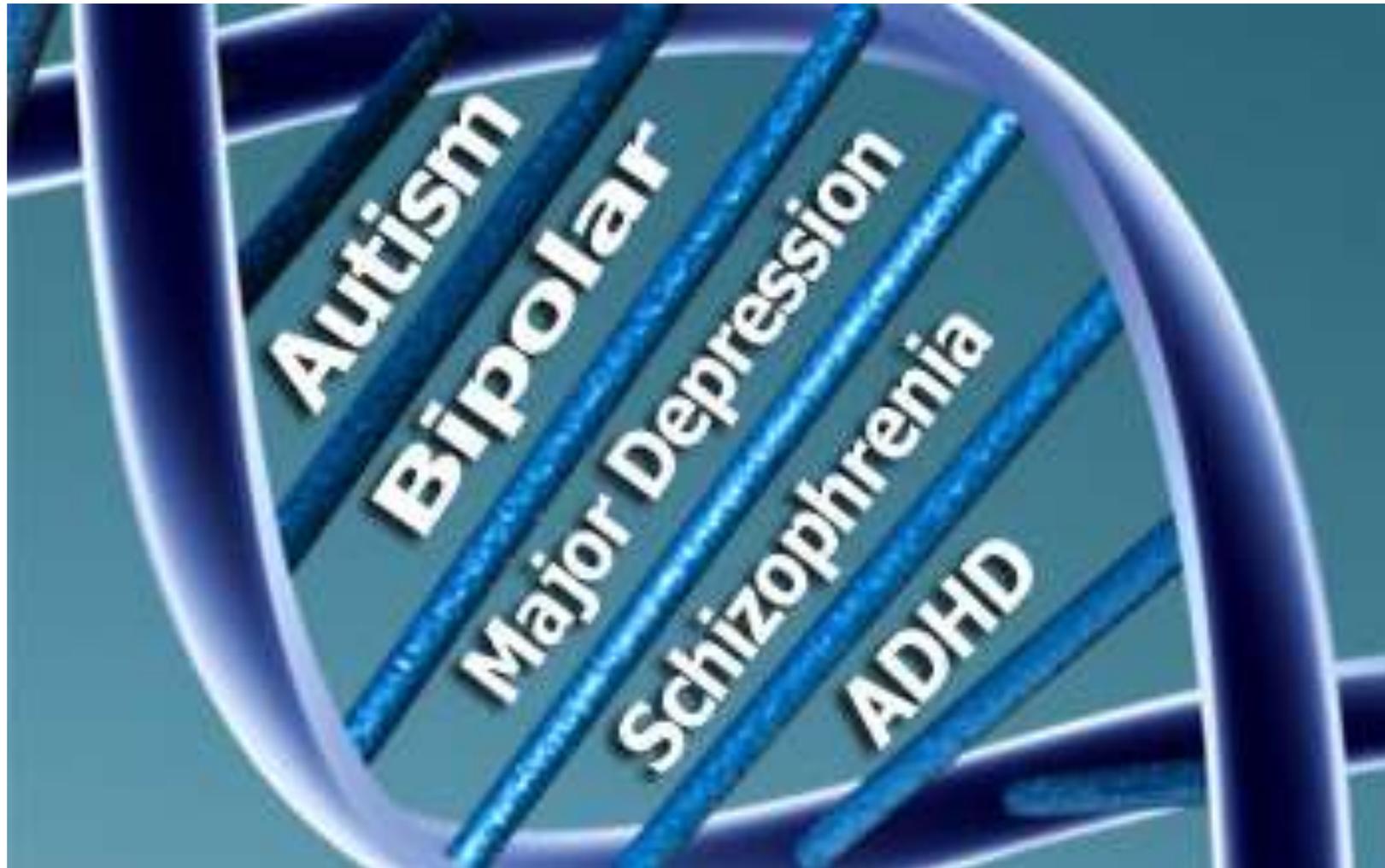


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Mental disorders as GENETIC DISEASES



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“One drunkard begets another”

Plutarch

- According to the scientific community, addictive behavior is a **GENETIC DISEASE**.
- *The general concept that addiction “runs in families” is beyond dispute.*
- However, the **addictive phenotype** could remain **hidden** because the **environmental factor** may be **protective** (e.g. the absence of exposure to drugs) even though a **large genetic load** may be present. *

*Volkow and Muenke, 2012.



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Precision Medicine Initiative.

January 2015



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Mental disorders and Precision Medicine in Psychiatry*

The aim of Precision Medicine is to enter a new era,
by changing our traditional concepts.

It has been defined as:

“an emerging approach for treatment and
prevention that takes into account each
person’s variability in genes, environment and
lifestyle”

* Toward Precision Medicine. Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease. National Research Council Committee on a Framework for Developing a New Taxonomy of Disease. Washington, DC, National Academies Press 2011).

Precision Medicine and DDs

Humans are unpredictable

Because of diversity in genotype and environment, *“One man's meat is another man's poison”*

Therefore, we must adopt a new approach and consider individual differences when we investigate the role of the genotype in the effect of substance abuse on the brain structure.



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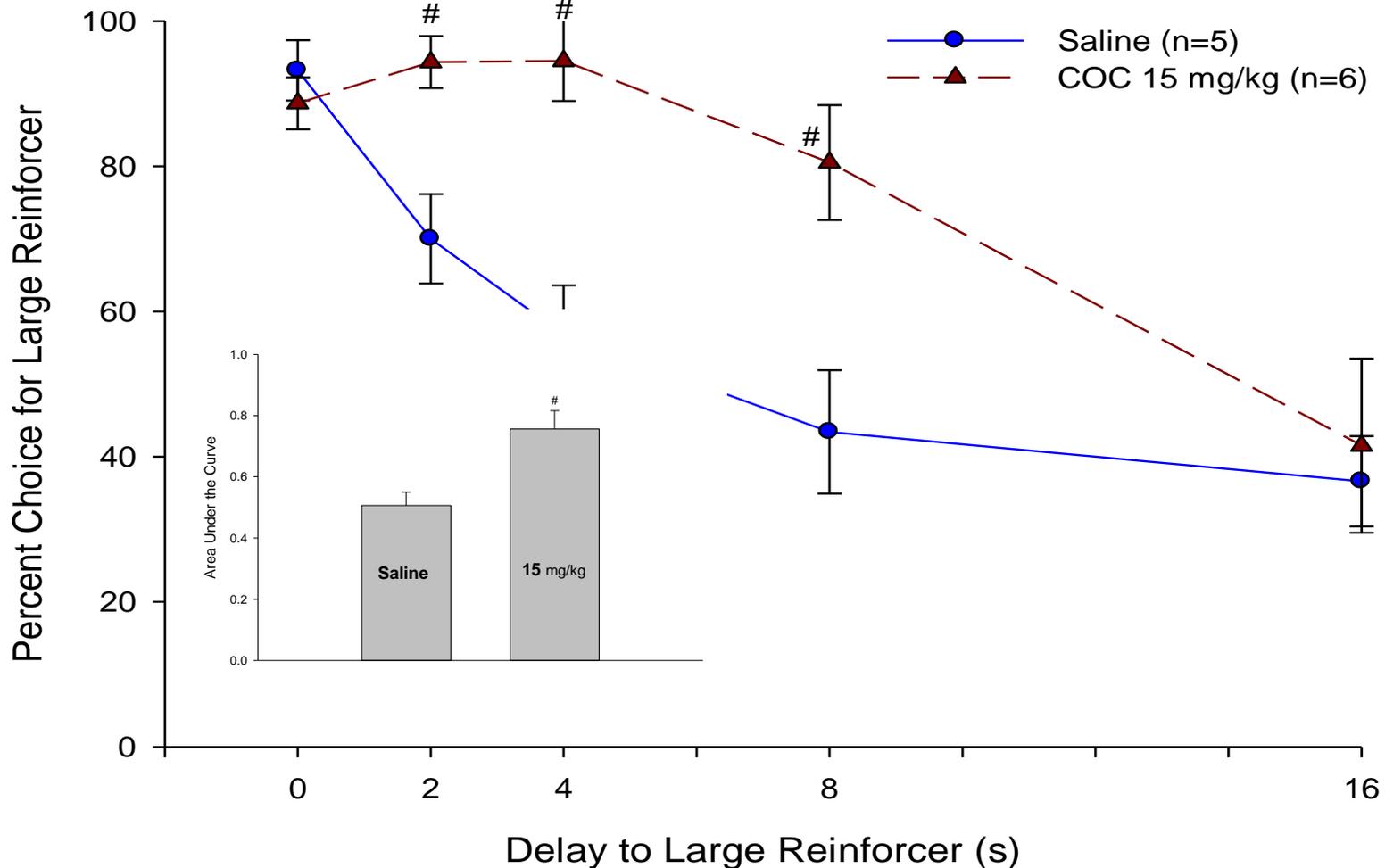
The same coffee and different brains



The same coffee and different brains

**Some people drink coffee to be
more awake and others to sleep
better**

Eliot Lawrence Gardner, Matthew W. Johnson, Natalie R. Bruner (2017) In Highly-Impulsive Rats, Acute Cocaine Use Decreased Impulsivity



In another study,

Impulsivity predicted addiction to cocaine in highly impulsive rats, but not their addiction to heroin*

* Belin D et al, 2015. Genes, Brain and Behavior (2016) 15: 74–88



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Will Dual Disorders lead to a new addictions paradigm?

OLD PARADIGM:

- Drug-induced neuroplasticity

NEW PARADIGM

- “individual-centered” approach that places individual variation as the focus of interest
- Does this recognize the connection between addiction and other mental disorders ?

Acad. Sci. 2011)

(Swendsen J and Le Moal M, Ann.N.Y.



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- **5- To summarize...:**



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In search of predictive endophenotypes in addiction: insights from preclinical research*

- Research approaches to addiction have evolved to reflect the ‘real world’:
- **Compulsive drug use goes beyond simple reinforcement mechanisms.**
- Research is going to identify distinctive neurobehavioral mechanisms and endophenotypes that predispose individuals to compulsive drug use.

- * Belin D et al, 2015. Genes, Brain and Behavior (2016) 15: 74–88



In search of predictive endophenotypes in addiction*

- However, research in active drug users is hampered by the difficulty in categorizing causal behavioral traits prior to the initiation of drug use.
- In fact addiction co-occurs with distinct pathological personality traits, other psychiatric disorders and cognitive impairment, that which we call Dual Disorders.
- * Belin D et al, 2015. Genes, Brain and Behavior (2016)



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Dual Disorders

These are disorders that begin at an early stage of development, possibly through the interaction of genetic, neurobiological and environmental factors.

They may be present with **different phenotypes**, such as addiction-related or other psychiatric symptoms, **at different stages of the lifespan***.

**Szerman N et al Addictive Disorders & Their Treatment 2013.*



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Dual Disorders

In the new clinical perspective we must always try to diagnose Dual Disorders/ Co-occurring Disorders in patients requiring care for addictive behavior and vice versa.

- One of the barriers to this goal is the lack of sensitivity and reliability of the current diagnostic criteria of mental disorders.



Dual Disorders

To conclude, the new paradigm of dual disorders tells us that we should treat the individual rather than the substance as we have done so far.

We need to rethink dual disorders in light of new evidence from Neuroscience research.



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Thank you for your attention

Merci beaucoup pour votre attention



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