

Neuroplasticity: An experienced addictionist reflects on clinical applications in recovery

Georgia Society of Addiction Medicine

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Al J. Mooney M.D.

- Chairman, Willingway Foundation
- Adjunct Associate Professor of Family Medicine,
University of North Carolina Chapel Hill



Neuroplasticity: The capacity of neuronal substance to change in response to environment and experience

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Neuroplasticity

- Introduction to the concept
- History of the idea and the science
- Present state of knowledge
- Barriers to application in practice
- Implications for clinical practice of addiction medicine

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History of brain plasticity

- Functional psychology - 1900
 - (William James, Edward Titchener)
- Identified by name – 1948
 - (Jerzy Konorski)
- Belief CNS was “fixed” – until 1970s
- Sensory substitution treatment – 1980
 - (Paul Bach-y-Rita)
- Cortical mapping – 1980s
 - (Michael Merzenich)
- Rodent barrel cortex – 1990s
- Brain-machine interface – 2000
- Stroke and TBI rehab - 2007

Categories of brain plasticity

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Types of neuroplasticity

- Negative
- Positive

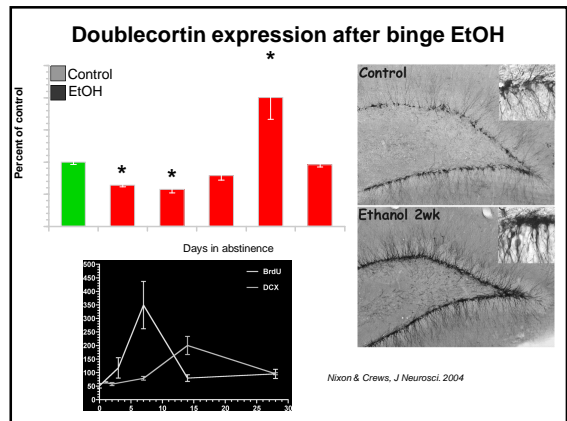
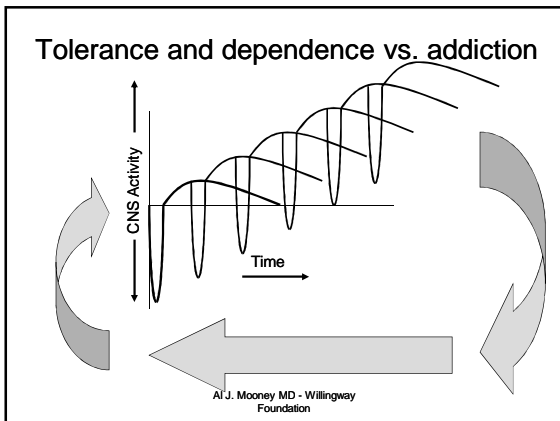
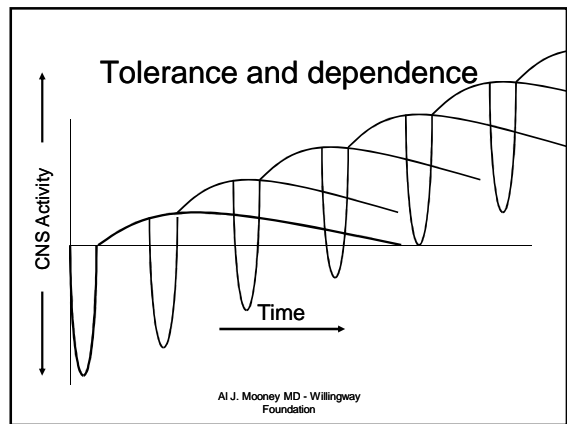
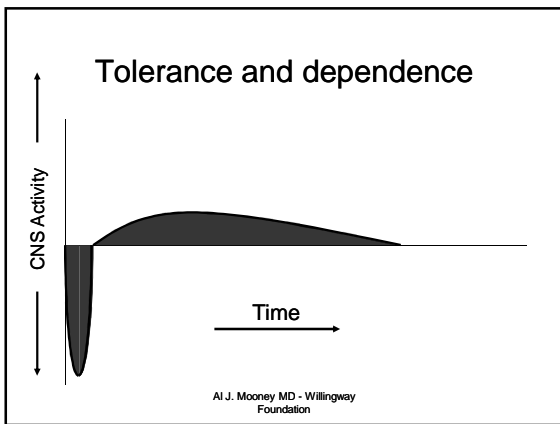
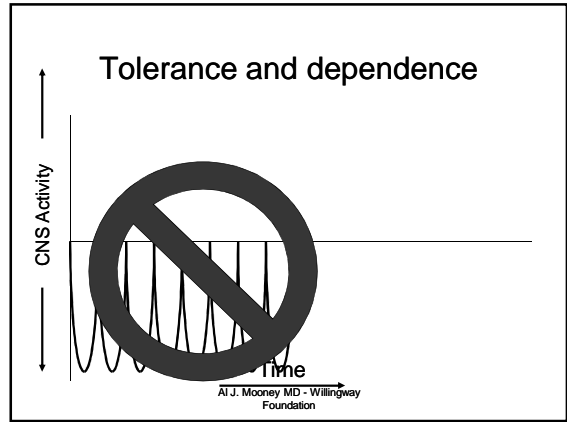
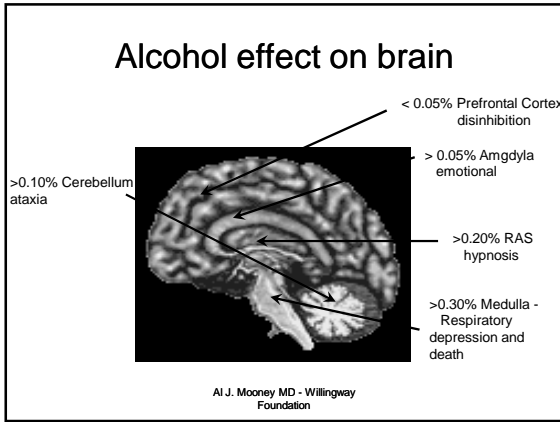
- Adding connections
- Removing connections (pruning)
- Sensitizing connections
- Desensitizing connections
- Adding neurons (neurogenesis)

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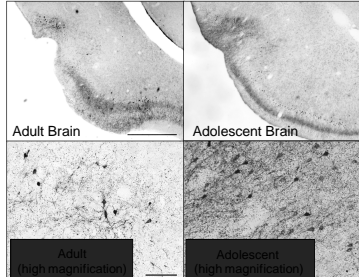
Forms of cortical neuroadaptation

- Expansion
 - Enlargement of functional areas
- Transfer
 - Function of one area moved to another region
- Substitution
 - One region that normally processes a certain sense becomes able to process a different sense
- Alternative processing
 - A task performed in one manner can be processed differently
- Regulation
 - Brain activity adjusts in response to external stimuli and assistance

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Binge Ethanol Induced Neuronal Death in Adult and Adolescent Perirhinal and Piriform Cortex

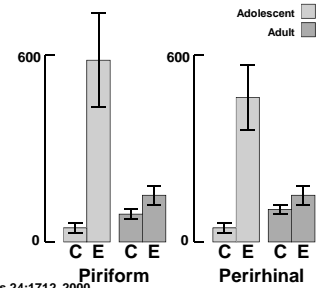
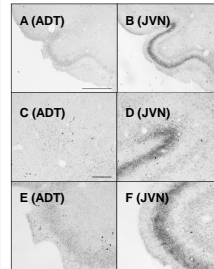


Silver staining (black areas) indicate neurodegeneration. Control animals have no silver staining.

Crews, et al., Alcoholism: Clin. Exp. Res. 24:1712, 2000

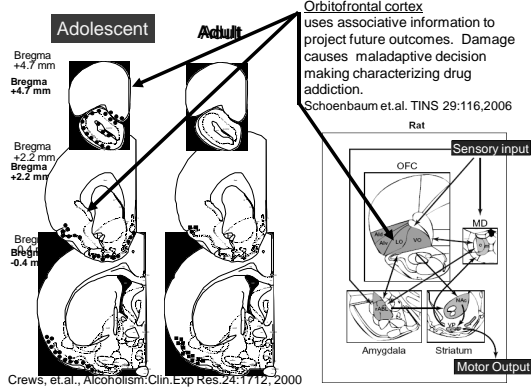
BINGE DRINKING DAMAGES THE ADOLESCENT BRAIN MORE THAN ADULT BRAIN
Comparison of Brain Damage Following 4 Day Binge Treatment of Adolescent (PN33) and Adult (PN80-90) Rats

Anterior Piriform and Anterior Perirhinal Cortex



Crews, et al., Alcoholism: Clin. Exp. Res. 24:1712, 2000

Schematic localization of Binge Drinking induced frontal brain damage.

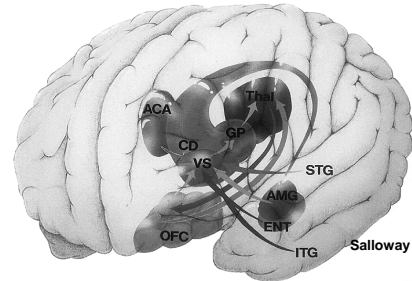


Crews, et al., Alcoholism: Clin. Exp. Res. 24:1712, 2000

Orbital Frontal and Anterior Cingulate Cortex control attention and risk evaluation: Impulsive and Compulsive behaviors are controlled.

Bechara et al 1994
Deficits in decision-making cognition in patients with OFC lesions.

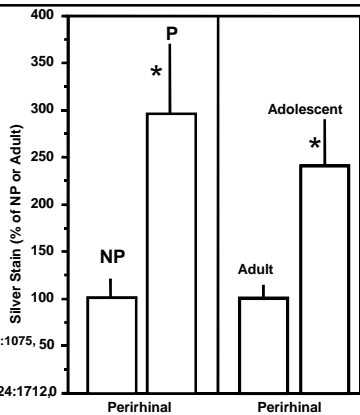
Wilson et al., 1996
Reduced pre-synaptic dopamine function in the striatum and altered 5HT metabolism in OFC of chronic methamphetamine abusers post-mortem



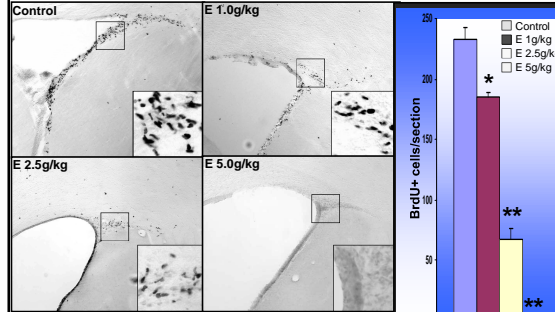
Volkow ND et al 1993, 1997 Reduced OFC metabolism and striatal D2 receptors in chronic cocaine abusers.

Binge Ethanol Induced Brain Damage Is Greater in Adolescent And Genetic Models of Alcoholism

Crews and Braun, Alcoholism: Clin. Exp. Res.:27:1075, 50 2003
Crews, et al., Alcoholism: Clin. Exp. Res. 24:1712, 2000



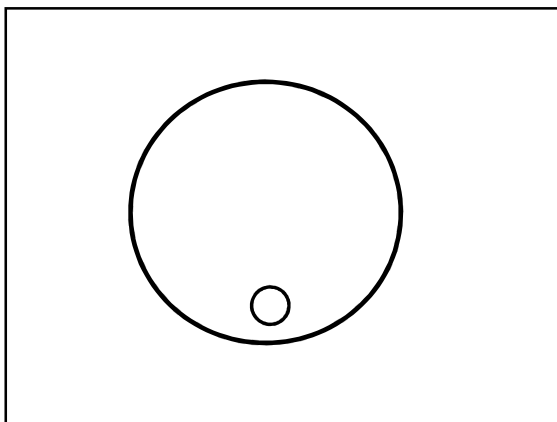
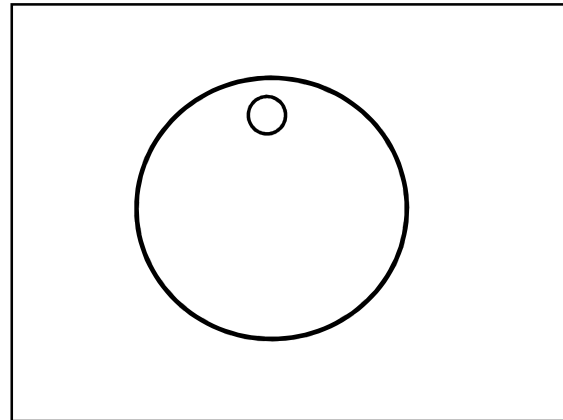
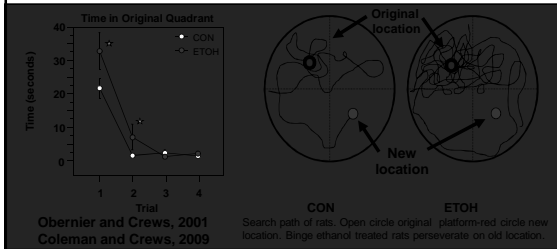
A single dose of ethanol Inhibits neurogenesis in adolescent rat forebrain



Ethanol at Binge drinking levels (5 drinks) markedly reduces neurogenesis.
Crews et al., 2006 Neuroscience

Binge Ethanol treated animals have persistent reversal learning deficits.

Ethanol binge treatment of adolescent mice or rats results in persistent reductions in reversal learning, an indicator of disrupted frontal cortical and learning networks. Adolescent ethanol results in adult relearning deficits in both Morris water maze and Barnes spatial learning maze.



Opportunities of neuroscience insights applied to addiction medicine

- Empowerment
- Lack of risk
- Costs
- Established applications
- Emphasis on health more than pathology

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Barriers to neuroplasticity research and application in practice

- Economics
- Medical tradition and structure
- Time

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Disease facts – The problem

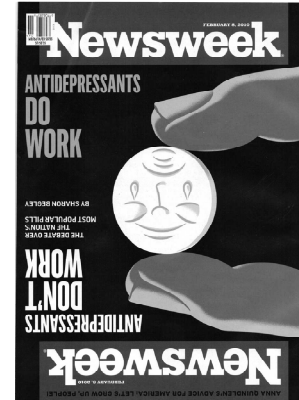
- Fatal illness
 - 100,000 deaths annually
 - YPLL = Cancer + Heart Disease
 - >80% unanticipated deaths in community mental health
- Number 1 Health problem
 - \$466 billion annual cost of NOT treating
 - No claims data to use for policy formulation
- 7% U.S. population afflicted
- ¼ of hospital admissions
- Family morbidity 43% (76,000,000)
- 100% increase in healthcare costs
- Primary cause of preventable birth defects
- Treatment yield of \$7 for \$1 expense
- \$39 Yield for each \$1 spent in medical settings
- Prevention reduces risk by 75%

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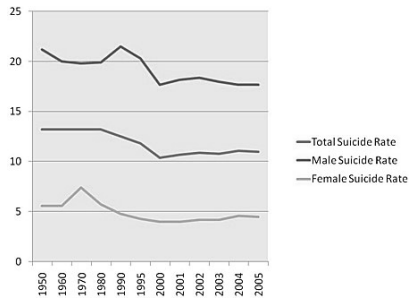
How to be “blinded by the evidence”

- Scientific methods are being used in ways that corrupt measurement of meaningful outcomes
 1. Adjust length of study to misrepresent outcome
 2. Measure effects to justify use of the medication
 3. Avoid measurement of side effects
 4. Emphasize statistical endpoints not relevant to clinical efficacy
 5. Pay researchers to publish positive outcomes
 6. Don't report negative results
 7. Publish research ghostwritten by marketing staff under physician bylines
 8. Avoid comparison with alternatives known to be effective
 9. Generalize data to populations excluded from study
 10. Infer efficacy by ignoring oscillations in illness severity
 11. Define a disease by a suspected drug effect

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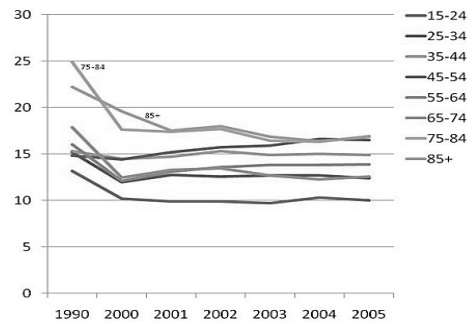


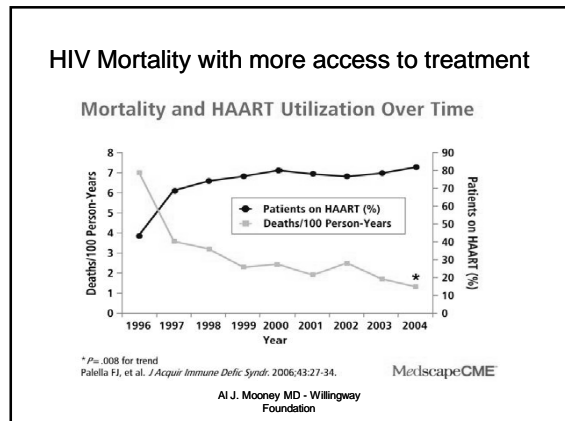
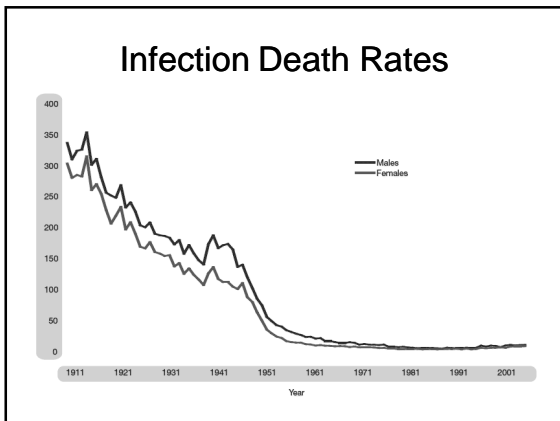
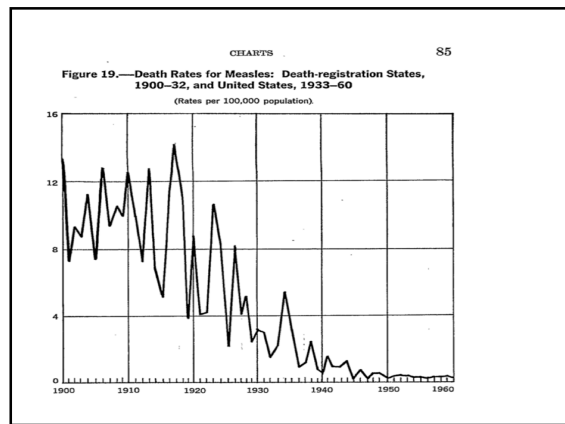
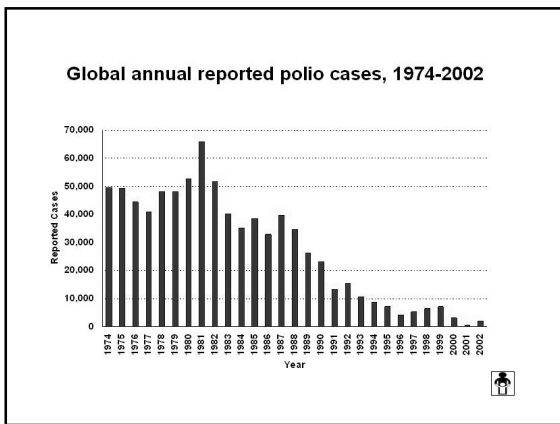
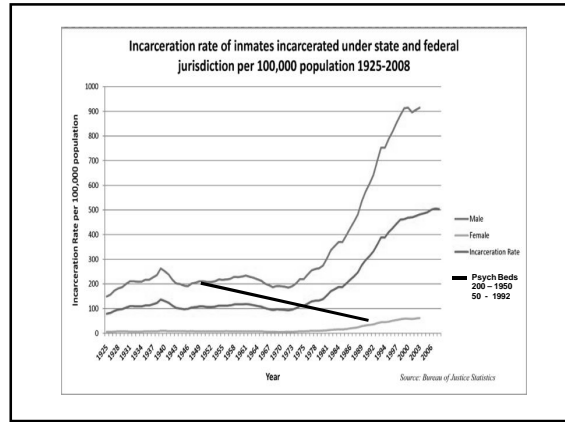
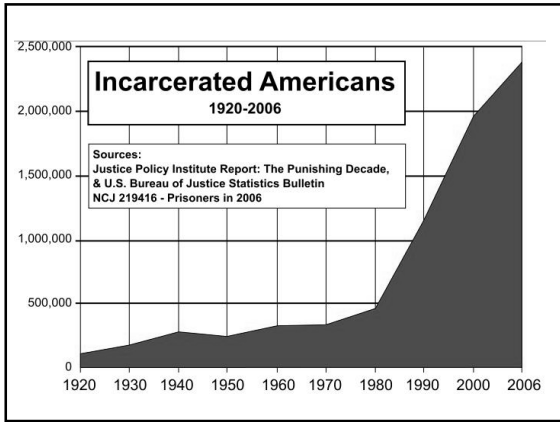
Suicide (1950-2005)



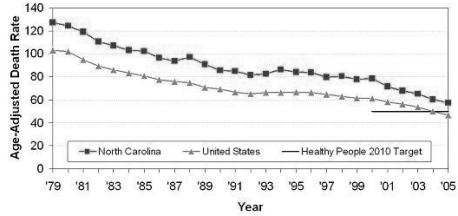
Sources: Centers for Disease Control and Prevention, National Center for Health Statistics. From *Health, United States, 2005*

Suicide by age (1990-2005)





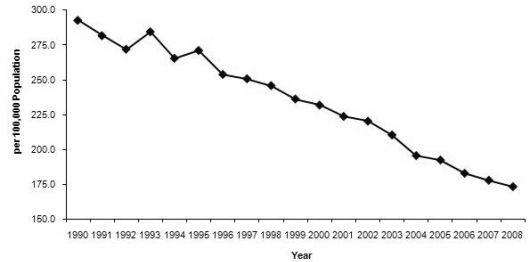
Stroke Death Rates, 1979-2005



1999-2006: ICD-10 codes I60-I69; 1979-1998: ICD-9 codes 430-434, 436-438 multiplied by comparability ratio of 1.0583. Rates per 100,000 population, age-adjusted to the 2000 U.S. standard population. Data Source: Compressed Mortality File, CDC Wonder.

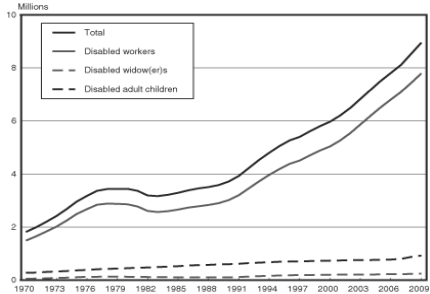
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Age Adjusted Mortality Rate For Heart Disease (per 100,000)



Kansas Department of Health and Environment <http://kc.kdhe.state.ks.us/kc/death.html>

Social Security disabled beneficiaries



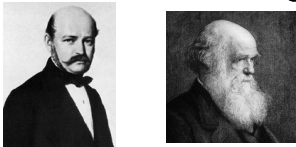
Annual Statistical Supplement to the Social Security Bulletin

Progress in scientific thought

- Evolutionary:
 - Evidence based advances
- Revolutionary:
 - Barriers from traditional ideas
 - Eg. Handwashing, flight, evolution, peptic ulcer disease/Marshall, cystic fibrosis

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Overcoming Barriers to Scientific Progress



Traditionism vs. new ideas



Geoffroy Saint-Hilaire

Georges Cuvier

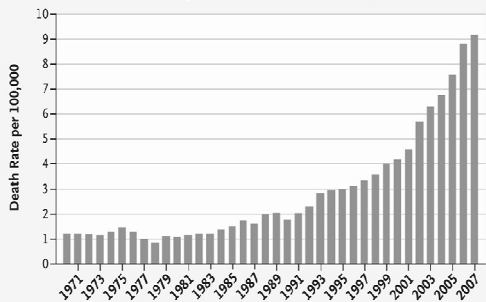
Overcoming Barriers to Scientific Progress



Addiction “progress”

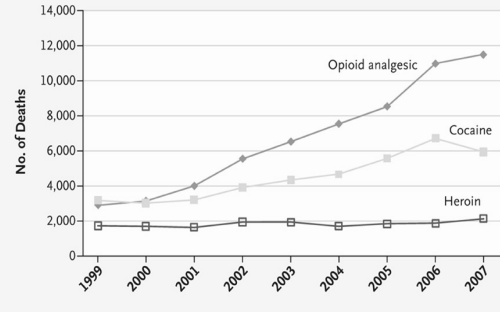
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A Deaths from Unintentional Drug Overdoses in the United States, 1970–2007



A Flood of Opioids, a Rising Tide of Deaths; *Okie*; NEJM November 18 2010; p1982

B Deaths from Unintentional Drug Overdoses in the United States According to Major Type of Drug, 1999–2007

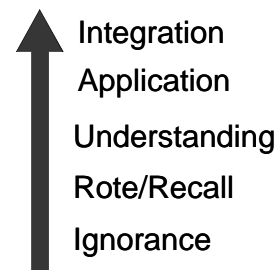


A Flood of Opioids, a Rising Tide of Deaths; *Okie*; NEJM November 18 2010; p1982

Practical application for recovery medicine

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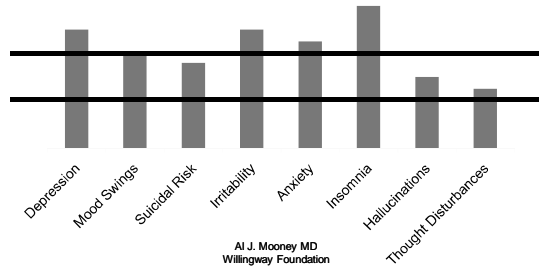
Levels of Expertise



**Drain the Swamp and see the stumps:
Clinical correlation of recent addiction
neuroscience and psychiatric co-morbidity**

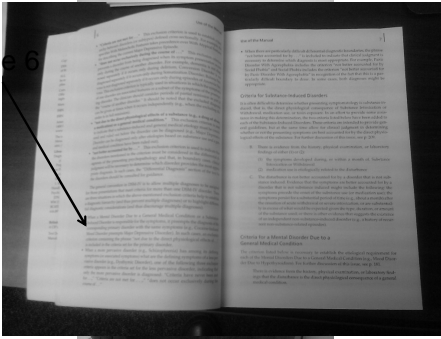


Stress, fatigue, sleep and sensory deprivation etc.
lower threshold for latent emotional symptoms



Addiction vs. DSM

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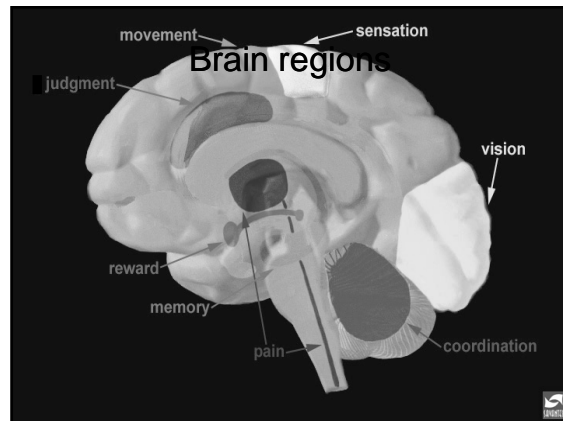
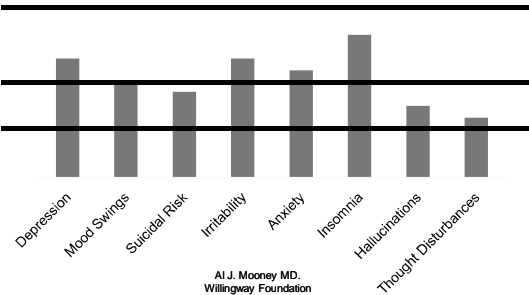
DSM exclusion criteria

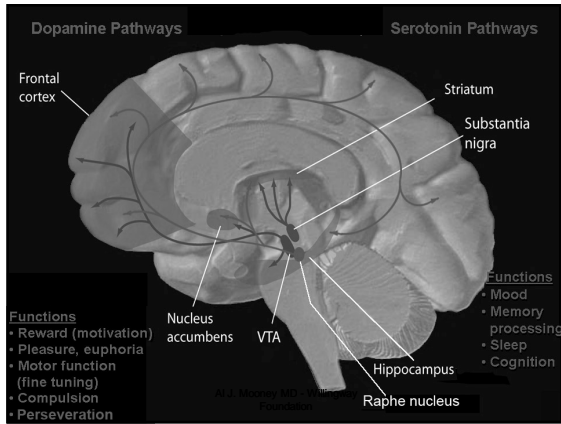
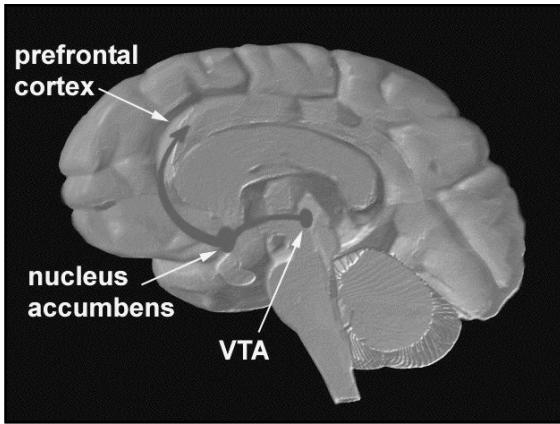
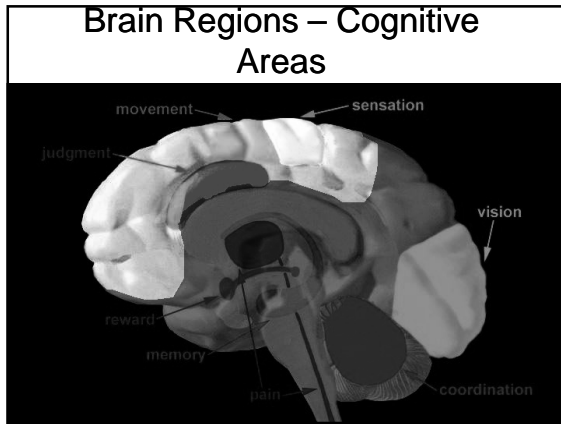
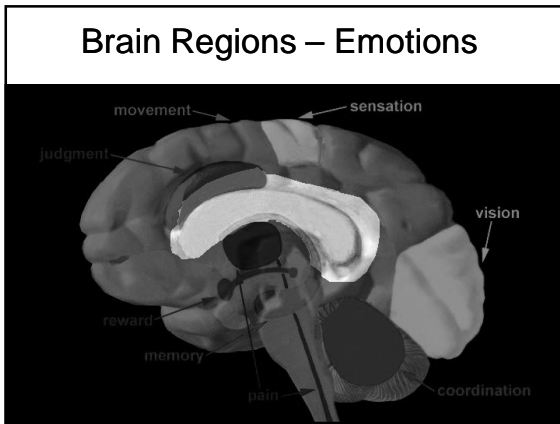
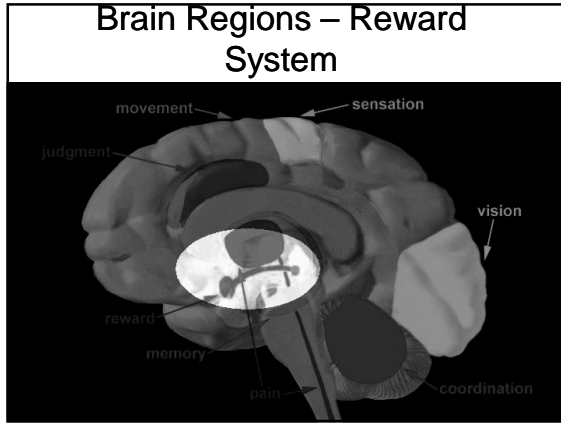
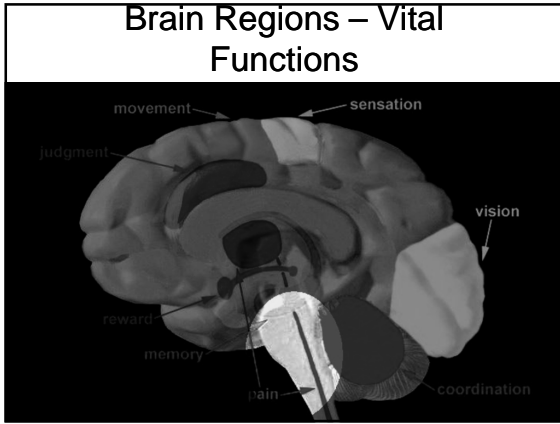
- When a Mental Disorder Due to a General Medical Condition or a Substance-Induced Disorder is responsible for the symptoms, it preempts the diagnosis of the corresponding primary disorder with the same symptoms (e.g., Cocaine-Induced Mood Disorder preempts Major Depressive Disorder). In such cases, an exclusion criterion containing the phrase "not due to the direct physiological effects of . . ." is included in the criteria set for the primary disorder.

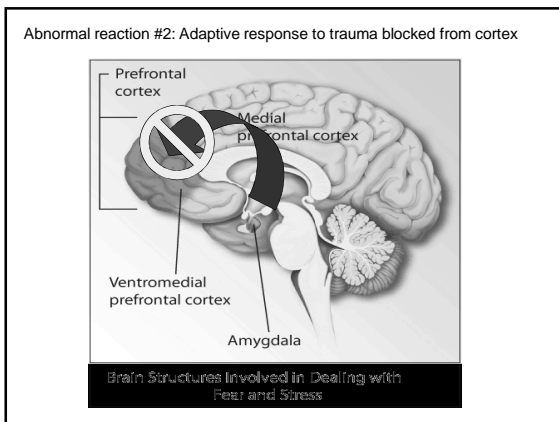
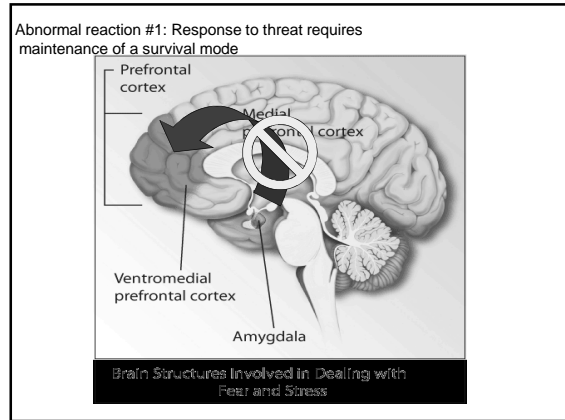
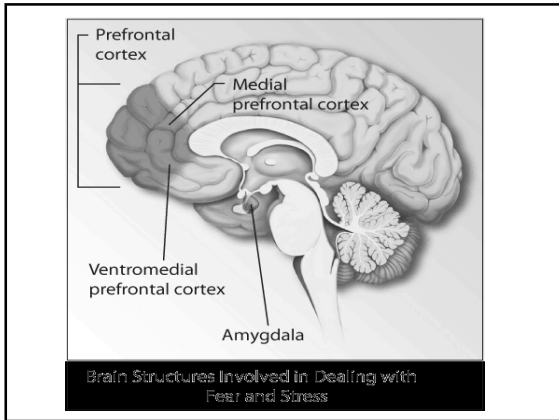
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**Impact of threshold changes of addiction on
mental co-morbidity**

(binge drinking and induction of innate immune genes create co-morbidity)
(and neuroplasticity of recovery helps resolve it)







Recovery goal?

- stay sober
- Sobriety is the condition of recovery, not the goal
- Life without a need for alcohol or drugs
- or
- Sanity returns and there is no need to drink or use drugs anymore

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Addiction medicine support using insights from neuroplasticity

- Motivate to utilize methods consistent with Alcoholics Anonymous principles
- Support developmental approach to recovery
- Medications may help engage recovery
- Short term minimum effective dosing (MED)
- Embrace life's challenges to promote emotional and social healing
- Insure safe healing environment
- Immersion in a recovery culture
- Reframe emotional & social failure as positive

Recovery expectations

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Promote success in recovery by engaging and linking its phases:

- First, save your life
- Next, do something worthwhile with it
- Finally, live as long as you can in recovery

The Recovery Book

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Recovery phases or zones

- > Phase I. Salvage life
- > Phase II. Make life worthwhile
- > Phase III. Prolong life

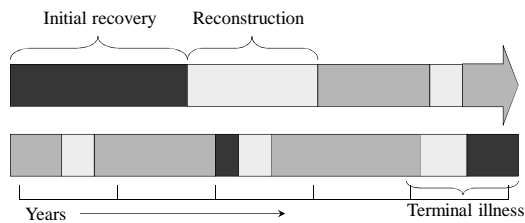
> Safety Zone

> Work Zone

> Comfort Zone

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Zones in the recovery timeline



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THE RECOVERY BOOK

Al J. Mooney MD
509 Midenhall Way
Cary, NC 27513
Mobile: 919 523 0569

Email: amooney@aol.com



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