


Substance Use Disorders


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 Recovery & Services Research



This must be California!



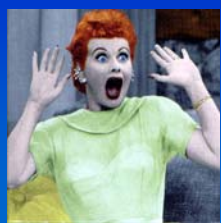
According to James Egar, public defender for Monterey County...



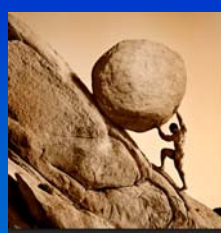
"In my 30-plus years of criminal law, more than anything else, substance abuse is driving the criminal justice system," Egar says. "Their crime may not have been a drug crime, but that's what's driving their life."

Monterey County Weekly, March 20-26, 2008

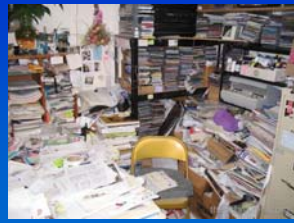
What a surprise!




Does it feel like this sometimes?



Getting behind?



Help is on the way!



Overview

- Neurobiology
- Risk factors and development
- Epidemiology
- Diagnosis
- Treatment and course

Key concepts

• Reinforcement	• Sensitization
• Behavioral regulation	• Hedonic regulation
• Salience	• Neuroadaptation
• Conditioned response	• Allostasis
	• Anticipation

Neurobiology of intoxication & addiction

Why do people take drugs?

Because we **want** to

Desire

- Why do we want?
- What do we want?
- How do we want?

Why do we want?



- Because if we didn't want anything, we wouldn't do anything (and then we would dehydrate, starve, get eaten, etc).
- ∴ **motivation** (desire) is essential to survival of the species.

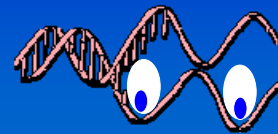
What do we want?

- Motivation developed through natural selection (evolution)
- We are motivated for whatever behavior maximizes survival of offspring.
- Includes safety, thirst, affiliation, sex, rock & roll, chocolate, lattes, etc.



In other words.....

- DNA has found a way to make us do its bidding!



OK, but **HOW**?

- Positive and negative feeling (affect) states provide reinforcement
- **Reinforcement** ⇔ after doing it, you are more likely to do it again
 - Positive – Negative – Punishment
- Feelings (affects) are not necessarily conscious (in fact, most are not)

Affect and Reinforcement

- A deficit state (e.g. hunger) is
 - experienced as painful, unpleasant
 - drives behavior to relieve it
- Relieving a deficit state* is experienced as pleasant, enjoyable

* (e.g. a Big Mac, or angel hair pasta with olive oil, garlic, capers, pine nuts, sun dried tomatoes, and wild mushrooms)



Incentive salience

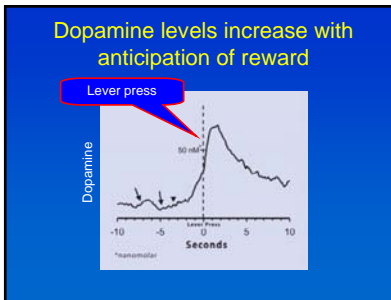
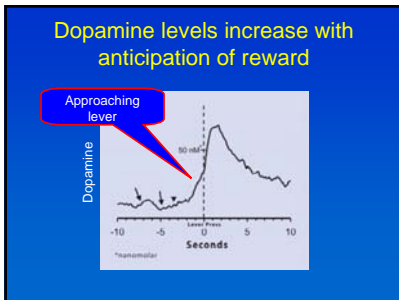
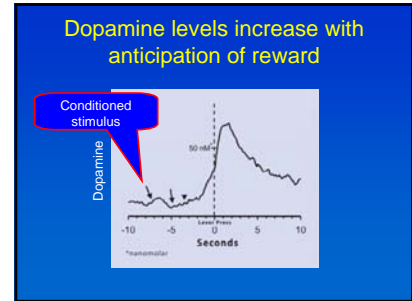
- **Anticipation** of reinforcement induces behavior intended to result in the desired event (seeking)
- Anticipation is a **conditioned response** and is itself reinforcing





Incentive salience

- **Preoccupation** is the cognitive correlate of anticipation or incentive salience
- **Seeking** the reinforcement is the behavioral correlate



Affect and Reinforcement

- Certain things are inherently reinforcing, e.g. sex, sweets, social affiliation, blues music, etc.

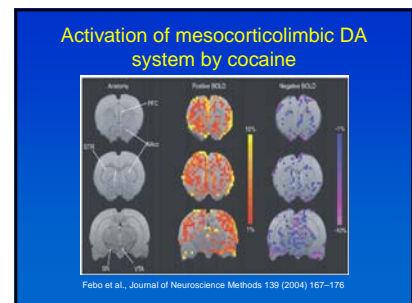
- A neutral state is non-motivating

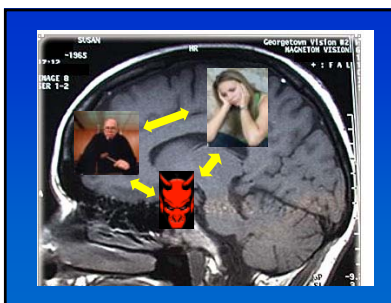
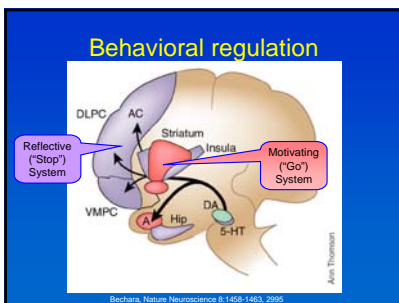
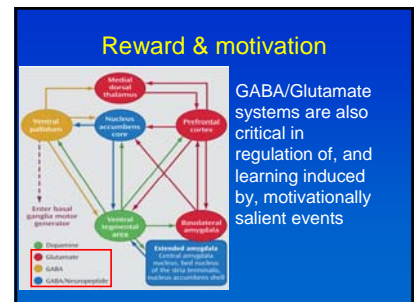
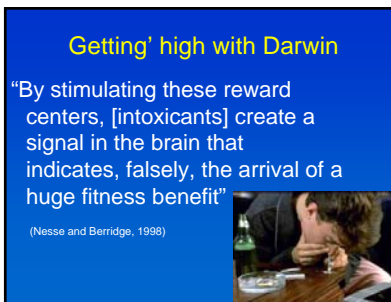
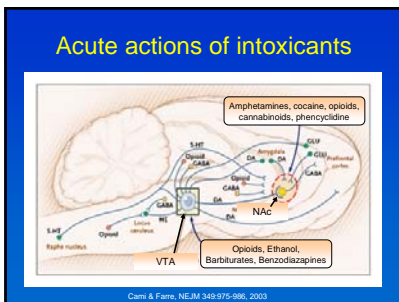
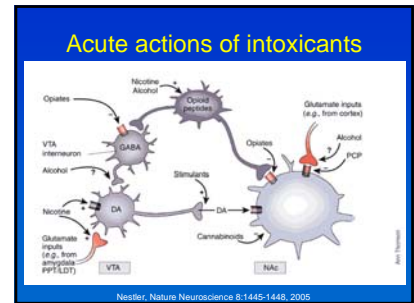
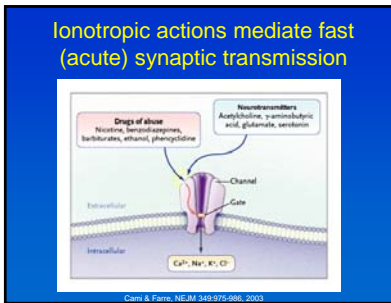
Reinforcement

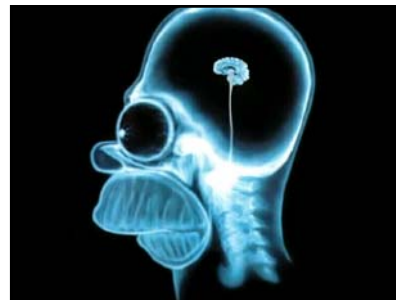
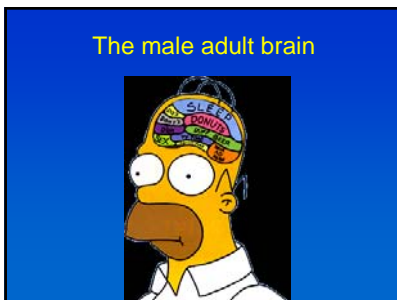
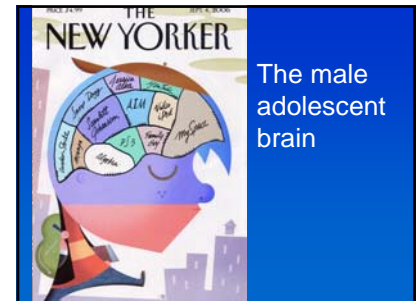
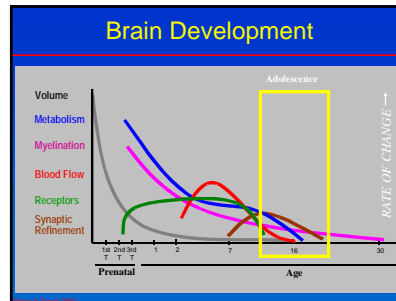
Dopamine & endogenous opioids are essential in regulation of reward (**hedonic regulation**).

Reinforcement

A key circuit involves fibers from the ventral tegmental area (VTA) that release dopamine (DA) in the Nucleus Accumbens (NAc).







What is addiction?

Addiction is wanting the wrong thing very, very badly.

It is a disorder of desire.

- ### Processes involved in substance use and addiction
- Reinforcement
 - Positive
 - Negative
 - Learning and memory
 - Classic conditioning
 - Operant conditioning
 - Incentive salience
 - Stress response system

Progression of addiction

First the (man) takes the drink
Then the drink takes the drink
Then the drink takes the (man)

"At first, I drank to feel good"
"Then, I drank to feel normal"
"Now, I drink to die"

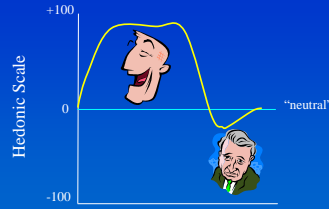
Progression of addiction

Functional homeostasis
↓
Use
↓
Binge intoxication
↓
Frequent heavy use
↓

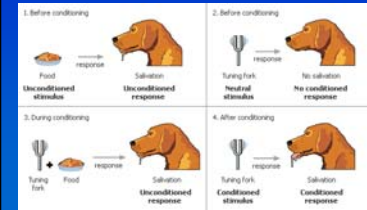
Progression of addiction

Frequent heavy use
↓
Neural and behavioral adaptation
↓
Deteriorating function
↓
Allostasis (sick homeostasis)

Acute Drug Effect



Classical conditioning



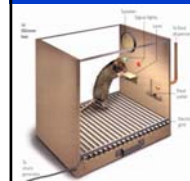
Classical conditioning

- Craving (incentive salience) invoked by conditioned cues
 - Smells - Paraphernalia
 - Music - Situations
 - Affect states
- Withdrawal states also are conditioned responses

Mmmmmmm...Beer!

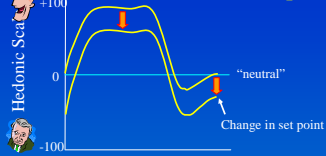


Operant conditioning



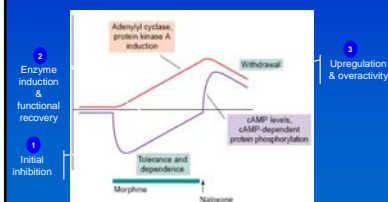
- Spontaneous action (e.g. lever pressing) results in reward (positive reinforcement) or removal of noxious experience (negative reinforcement)
- Shapes behavior through learning & memory

Counter-adaptation

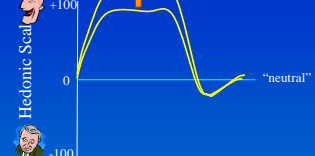


Counter-adaptation (tolerance) occurs after a period of prolonged use. It leads to escalation in use to achieve an effect and increasing dysphoria.

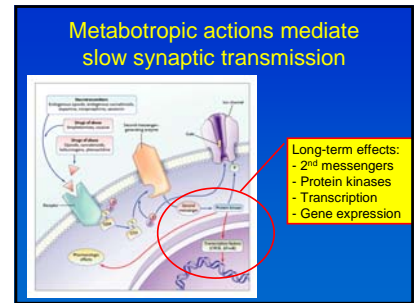
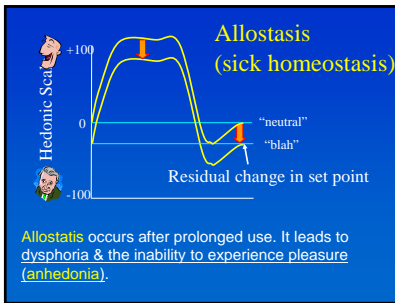
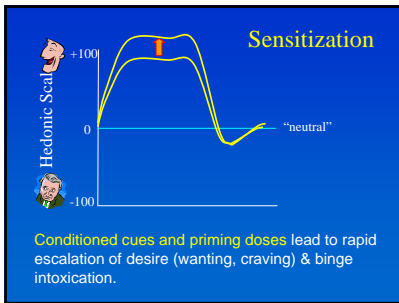
Upregulation of cAMP in opioid tolerance & dependence



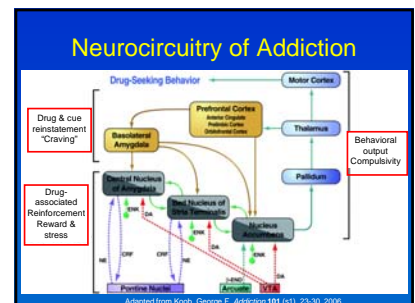
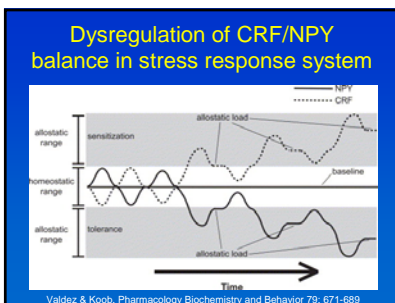
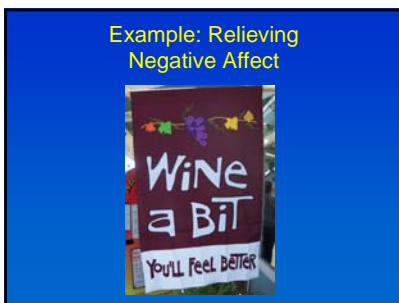
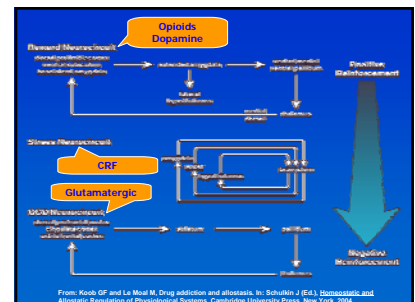
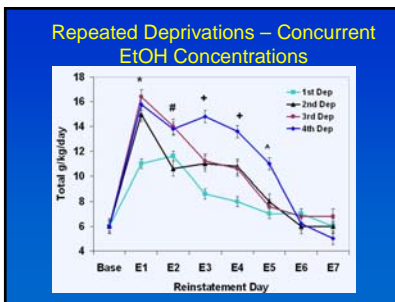
Sensitization

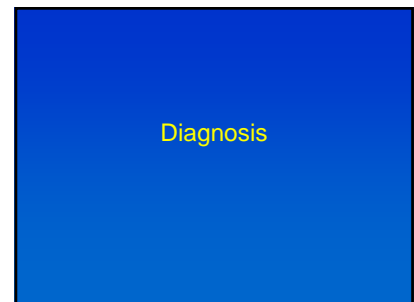
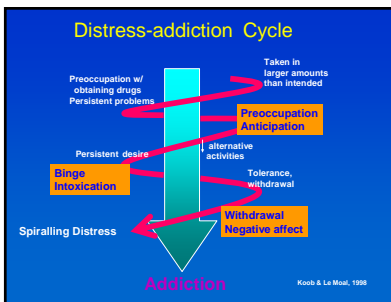
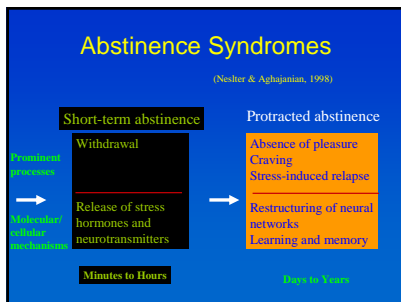
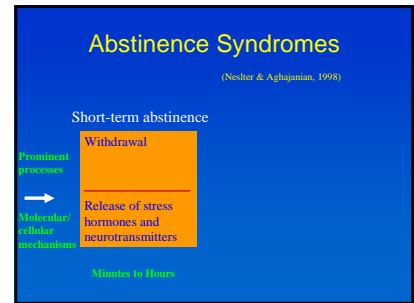
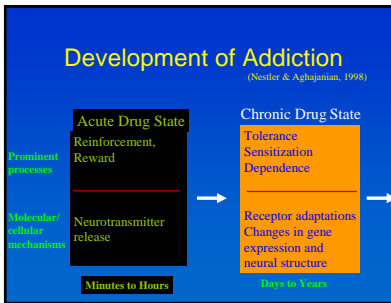
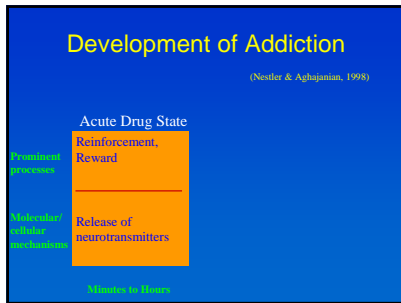


Sensitization occurs after a period of abstinence. It leads to craving and rapid reinstatement of addiction.



- ### Molecular/cellular adaptations
- Functional (physiologic)
 - Second messengers (cell energy systems)
 - Lasting hours to days
 - Structural (gene expression)
 - Change cell protein
 - Permanent



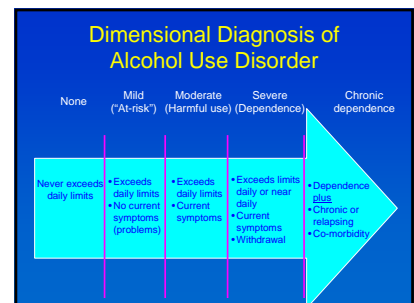


Definitions

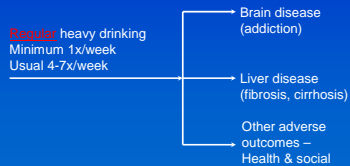
- Standard drink:** typical US drink containing about 14 grams of absolute alcohol
 - 12 oz. beer
 - 5 oz. wine (5 drinks per bottle)
 - 1.5 oz. shot of 80 proof spirits (22 drinks/liter)

Definitions

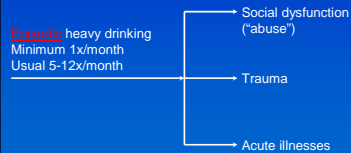
- At-risk (heavy) Drinking:** exceeding NIAAA recommended maximum daily limits
 - Men: 5+ drinks in a day
 - Women: 4+ drinks in a day
- Regular heavy drinking:** monthly +
- Alcohol use disorder:** regular heavy drinking causing symptoms &/or dysfunction



Risk model of regular heavy drinking and adverse outcomes



Risk model of episodic heavy drinking and adverse outcomes



Alcohol Dependence Syndrome

Edwards and Gross (1976). British J. of Addictions 1:1058-1061

- Narrowing of the drinking repertoire
- Salience of drink-seeking behavior
- Increased tolerance to alcohol
- Repeated withdrawal symptoms
- Relief or avoidance of withdrawal symptoms by further drinking
- Subjective awareness of compulsion to drink
- Reinstatement after abstinence

DSM IV Dependence

- Common Features:
 - Maladaptive pattern of use
 - Clinically significant impairment or distress
- + 3/7 criteria w/i 12 mo period

Dependence focus 1: Loss of control (4)

- Larger amts or longer time
- Persistent desire or unsuccessful attempts to control



Dependence focus 1: Loss of control (4)

- Great deal of time spent on anticipation/use/recovering
- Important alternative activities reduced or given up



Dependence focus 2:

Adverse consequences (1)

Persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by the substance



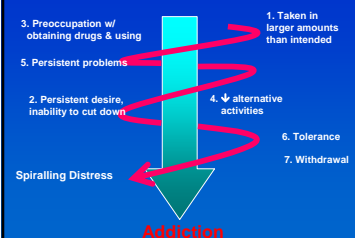
Dependence focus 3:

Physiological dependence (2)

- Tolerance
- Withdrawal

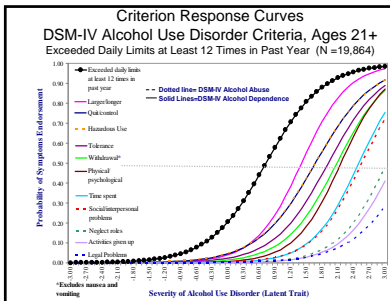


DSM-IV Diagnosis

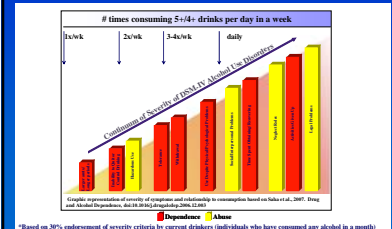


DSMIV Abuse

- A. Common features +
- B. Persistent problems
 - Role failure – Legal
 - Physical hazard – Social
- C. Never met criteria for dependence



How Hazardous Drinking Relates to DSM-IV Alcohol Abuse and Alcohol Dependence – A Model*



Progression of dependence

- Early symptoms
 - Larger/longer
 - Persistent desire to cut down/quit
 - Drink driving (physically hazardous use)
 - Heavy drinking 1-3 times per week
 - 3-6 drinks per drinking day average

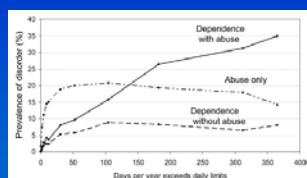
Progression of dependence

- Moderate symptoms
 - Increasing time spent drinking
 - Decreased time spent on other activities
 - Use despite psychological/physical consequences
 - Interpersonal problems
 - Heavy drinking 4+ days per week
 - 5-8 drinks per drinking day

Progression of dependence

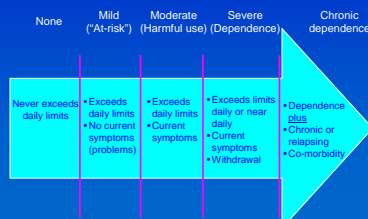
- Severe symptoms
 - Tolerance
 - Withdrawal
 - Role failure
 - Legal problems
 - Daily/heavy daily heavy drinking
 - Averaging 12 drinks/drinking day

43% of daily/near daily heavy drinkers do not meet criteria for an alcohol use disorder



Dawson et al., Alcohol Clin Exp Res 29:902–908, 2005

Dimensional Diagnosis of Alcohol Use Disorder



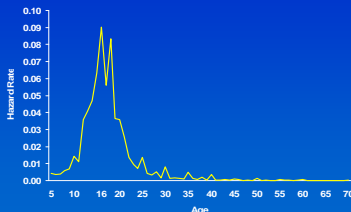
Epidemiology

Initiation of drug use

- Ages 12-18
- Peer groups, siblings
- Early use (<15) predicts problems later

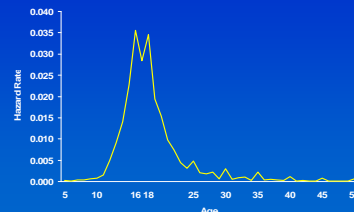


First Use of Any Tobacco



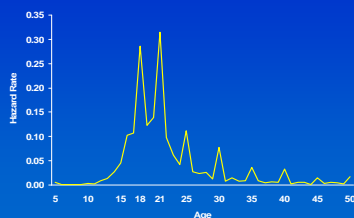
Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

First Use of Cannabis



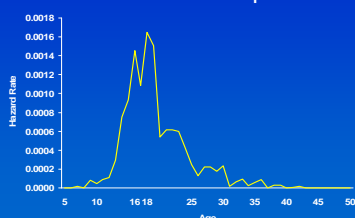
Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

First Use of Alcohol



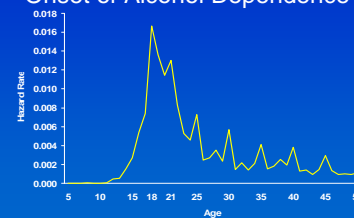
Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

Onset of Cannabis Dependence



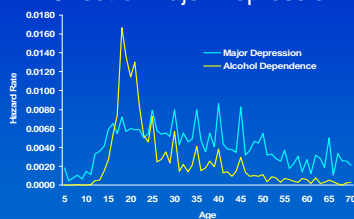
Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

Onset of Alcohol Dependence



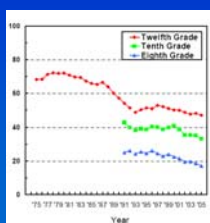
Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

Onset of Major Depression



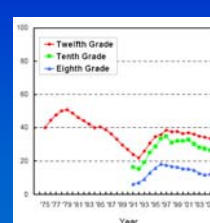
Source: NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

Use of alcohol past 30 days



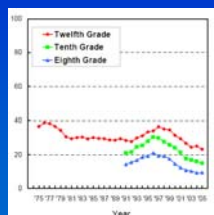
Source: Monitoring the Future Study

MJ use past 12 months



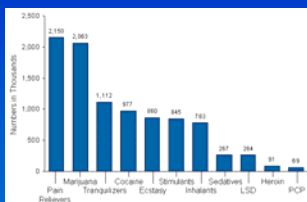
Source: Monitoring the Future Study

Cigarette use past 30 days



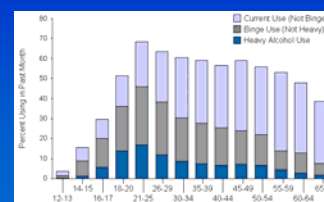
Source: Monitoring the Future Study

Past Year Initiates for Specific Drugs among People 12 +: 2006



NSDUH 2006

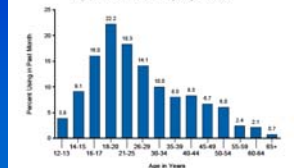
Drinking patterns by age



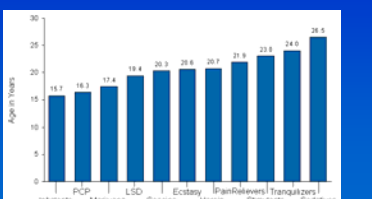
NSDUH 2006

Drug Use Peaks Early

Figure 2.3 Past Month Illicit Drug Use among Persons Aged 12 or Older, by Age: 2006

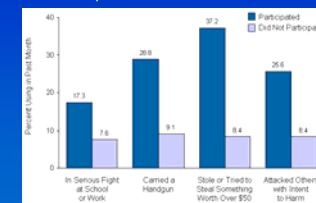


Age at First Use for Specific Drugs, Past Year Initiates Ages 12-49: 2006



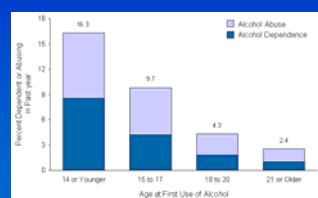
NSDUH 2006

Past Month Substance Use among Youths Aged 12 to 17, by Participation in Fighting and Delinquent Behavior in the Past Year



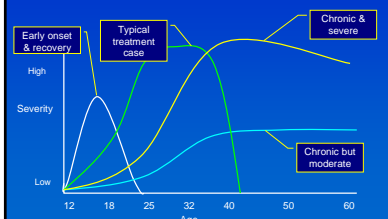
NSDUH 2006

Alcohol Use Disorder in the Past Year among Adults Aged 21+ by Age at First Use of Alcohol

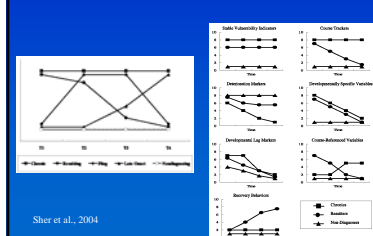


NSDUH 2006

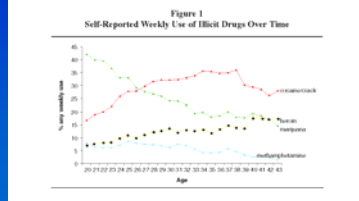
Heterogeneity of Course



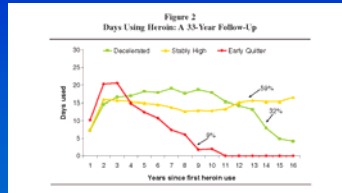
Life course approaches



Life course of drug use



Life course of heroin use



Episodic nature of alcohol use disorders (AUD)

- >70% have one episode only
- Average episode lasts 4 years or less
- Those who have >1 average 5 episodes
- Episodes are of decreasing length

Hasin et al., Arch Gen Psychiatry 2007

Past month use of intoxicants (millions of persons age 12+, US)

- Marijuana: 14.8
- All other drugs: 9.6
- Psychotherapeutics: 7.0
- Pain relievers: 5.2
- Cocaine: 2.4
- Methamphetamine: 0.7
- Heroin: 0.3
- Oxycontin: 0.3
- (Alcohol: 140)

Source: NSDUH

12-Month and Lifetime Prevalence Rates - US

- Alcohol dependence
 - 12 Mo: 4.3%
 - Lifetime: 12%
- Other (non-nicotine) drug dependence
 - 12 Mo: 0.6%
 - Lifetime: 2.7%

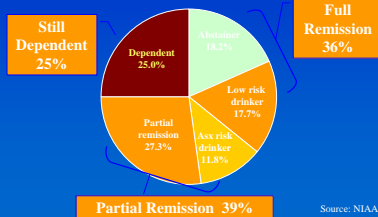
Hasin et al., 2007; Compton et al., 2007

Episodic nature of alcohol use disorders (AUD)

- >70% have one episode only
- Average episode lasts 4 years or less
- Those who have >1 average 5 episodes
- Episodes are of decreasing length

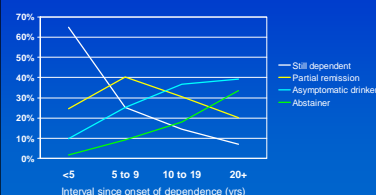
Hasin et al., Arch Gen Psychiatry 2007

Current Status of Adults with Prior to Past Year Dependence



Source: NIAAA

Many people with SUDs remit spontaneously



NESARC, 2003

Severity predicts disability

DSM-IV Diagnosis	Mean SF-12 score
Abuse	49.8
Dependence diagnosis	47.3
3 criteria +	49.3
4 criteria +	47.4
5 criteria +	43.3
6 criteria +	42.3
7 criteria +	42.3

Hasin et al., Arch Gen Psychiatry 2007

Subtypes of alcohol dependence

- Cluster 1: Young adult
- Cluster 2: Functional
- Cluster 3: Intermediate familial
- Cluster 4: Young antisocial
- Cluster 5: Chronic severe

Moss et al., Drug Alc Depen 2007

Subtypes of alcohol dependence

Cluster	%	Age Onset	DSM-IV Criteria	Max # drinks	Sought help (%)
1. Young adult	31.5	19.6	3.9	13.8	18.7
2. Functional	19.4	37.0	3.6	10.0	17.0
3. Intermediate familial	18.8	32.0	3.7	9.8	26.9
4. Young antisocial	21.2	15.5	4.7	17.1	34.4
5. Chronic severe	9.2	15.9	5.4	15.4	66.0

(Moss et al., Drug Alc Depen 2007)

Subtypes of alcohol dependence

Cluster	%	Age Onset	DSM-IV Criteria	Max # drinks	Sought help (%)
1. Young adult	31.5	19.6	3.9	13.8	18.7
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5. Chronic severe	9.2	15.9	5.4	15.4	66.0

(Moss et al., Drug Alc Depen 2007)

1/3 have mild self-limiting course in youth

Subtypes of alcohol dependence

Cluster	%	Age Onset	DSM-IV Criteria	Max # drinks	Sought help (%)
1. Young adult	31.5	19.6	3.9	13.8	18.7
2. Functional	19.4	37.0	3.6	10.0	17.0
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4. Young antisocial	21.2	15.5	4.7	17.1	34.4
5. Chronic severe	9.2	15.9	5.4	15.4	66.0

(Moss et al., Drug Alc Depen 2007)

40% have later-onset, moderate form with psychopathology

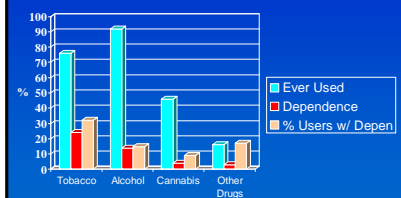
Subtypes of alcohol dependence

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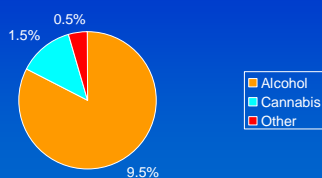
(Moss et al., Drug Alc Depen 2007)

1/3 have early onset, severe chronic dependence

Use, Dependence & Risk

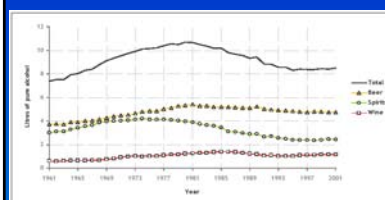


12 mo prevalence of SUDs in US



Grant et al., Arch Gen Psych 2004;61:807-816

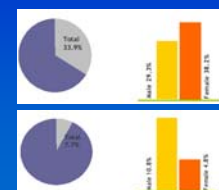
US: per capita consumption



US: Drinking patterns

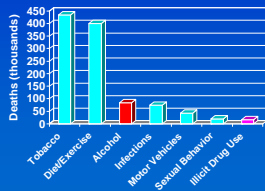
Abstainers
33.9%

Dependence
7.7%



US Causes of Death, 2000

Source: Mokdad et al., *JAMA*. 2004;291:1238-1245



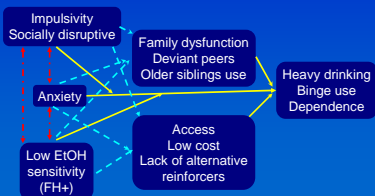
Risk factors

Risk Factors

- Gender
- Psychopathology
- Family history
- Family & social environment
- Culture & Ethnicity
- Geographical Region

Gene-environment interaction

Endophenotypes Environment Clinical Phenotype



Gender

- Alcohol dependence M/F:2.5/1
- Illicit drug dependence M/F:2/1

Personality

- Traits
 - Extroversion
 - Risk taking
 - Anxiety
- Disorders
 - Conduct disorder/ASPD (7X risk)
 - All personality disorders confer added risk (2-4X)

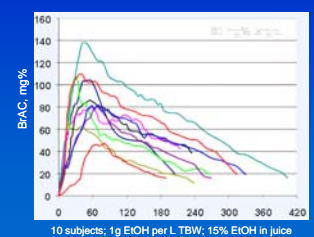
Axis I Disorders

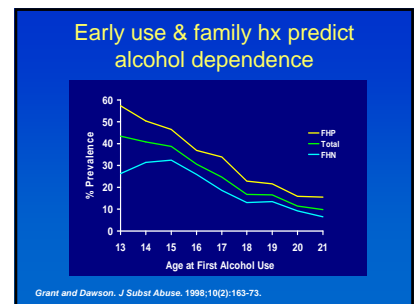
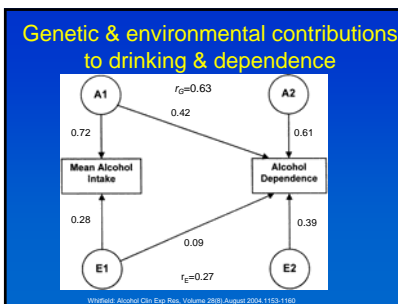
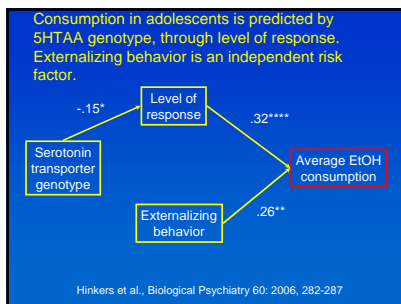
- ADHD
- Bipolar disorder
- Depression
- Schizophrenia
- Social phobia
- PTSD

Family History

- Genetics similar to other common complex diseases (heart disease, diabetes, and asthma)
- About 50% genetic, 50% environment
- Environmental parent substance use not predictive
- Low alcohol responsivity predicts for dependence

Variation in Brain Exposure to Alcohol





Family: Reduced Risk

- Male parent @ home
- Parental involvement
- Religiosity
- Concept of scaffolding

Social environment

- Deprivation
- Alternative reinforcers
- Access
- Cost

Ethnicity

- Whites > African Americans
- US Latinos overall comparable
- Lower risk among Chinese Americans
- Native Americans -> high rates of alcohol dependence and abstinence

Geographical Region (US)

- Highest risk: West
- Lowest risk: South
- Intermediate: Midwest, East

Treatment

ON THE OTHER HAND, YOU'VE GOTTA GIVE HIM CREDIT FOR HONESTY

The problem is daunting



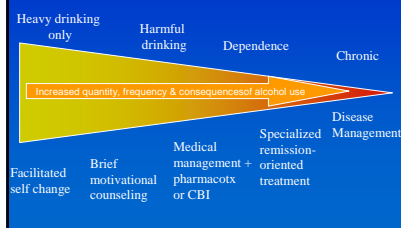
We are making progress...



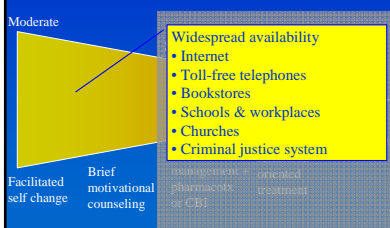
Dimensional Diagnosis of Alcohol Use Disorder

None	Mild ("At-risk")	Moderate (Harmful use)	Severe (Dependence)	Chronic dependence
Never exceeds daily limits	• Exceeds daily limits • No current symptoms (problems)	• Exceeds daily limits • Current symptoms	• Exceeds limits daily or near daily • Current symptoms • Withdrawal	• Dependence plus • Chronic or relapsing • Co-morbidity

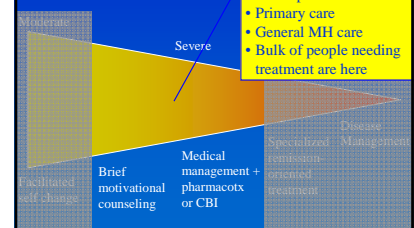
Extended Continuum



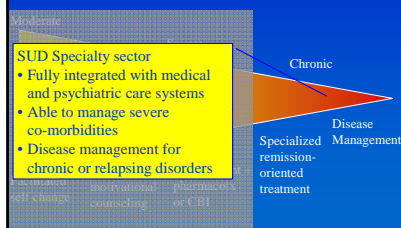
The extended continuum



The extended continuum



The extended continuum

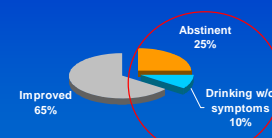


Brief interventions by physicians are effective

- Average reduction in drinking of 25% after one year
- Very brief (5") intervention is effective in primary care settings
- Equally effective for men and women
- Use empathic, non-judgmental approach (e.g. FRAMES)

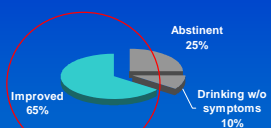
Ballosteros et al., ACER 28: 608-618, 2004

12 Month Treatment Outcomes: Full Remission in 35%



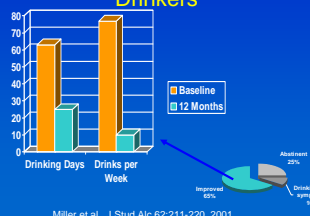
Miller et al., J Stud Alc 62:211-220, 2001

12 Month Treatment Outcomes: Partial Remission Among Drinkers



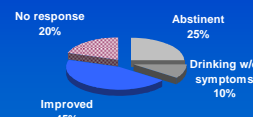
Miller et al., J Stud Alc 62:211-220, 2001

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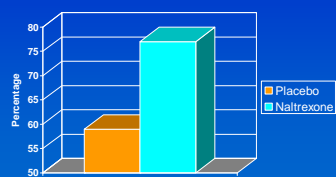
Miller et al., J Stud Alc 62:211-220, 2001

12 Month Treatment Outcomes: Lack of Response (estimate)

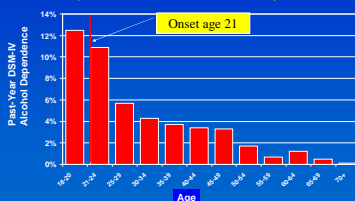


M. Willenbring: Private communication

Good clinical outcome: Naltrexone + medical management support

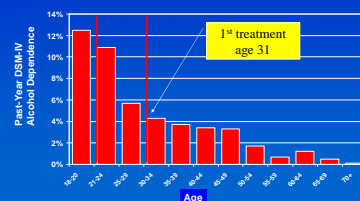


Prevalence of Alcohol Dependence Peaks Early



Grant, B.F. et al., Drug and Alcohol Dependence, in press 2004.

1st Treatment in US is 8-10 years later



Grant, B.F. et al., Drug and Alcohol Dependence, 2004.

Treatment

- What is treatment?
- "treatment" or "Treatment!"?
- Keep your eye on the ball (the result is more important than the method to achieve it)
- Monitor a long time

Specialty treatment

- Social and Behavioral Treatment
 - Brief motivational counseling
 - Cognitive-Behavioral
 - 12-Step (MN Model)
 - Motivational Interviewing
 - Contingency management
- Pharmacological treatment
 - Methadone, LAAM, Buprenorphine
 - Naltrexone, acamprosate/tamabuse

General trends in SUD tx

- Less confrontation, more empathic
- Focus on motivation
- Integrating pharmacotherapy
- Treatment in primary care
- Combining treatments for CD, medical, and psychiatric d/o
- Disease management for chronically ill

Evidence Based Treatments

- Alcohol dependence
 - Pharmacotherapy & brief medical support
 - Specialty counseling (rehab)
 - OP & residential equally effective
- Cannabis
 - Primarily adolescents
 - Multi-modal specialty treatment
- Cocaine/Amphet
 - Specialty counseling
 - Residential better if complicated

Evidence Based Treatments

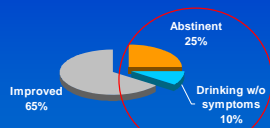
- Heroin/Opiates < 1 year
 - Specialty counseling +
 - Naltrexone (monitored or injectable)
- Heroin/Opiates > 1 year
 - Maintenance on methadone or buprenorphine
 - Abstinence approaches not effective

Specialty treatment is Effective

- Studies totalling 8,389 clients seeking treatment for alcohol dependence
- 83% follow-up rate
- One year follow up after single treatment
- Psychosocial treatment ranging from weekly psychotherapy to intensive residential care for 4 weeks

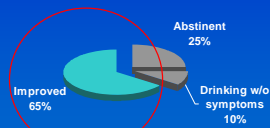
Miller et al., J Stud Alc 62:211-220, 2001

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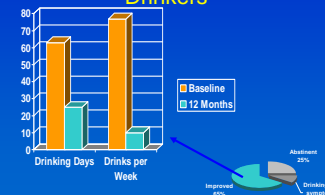
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12 Month Treatment Outcomes: Partial Remission Among Drinkers



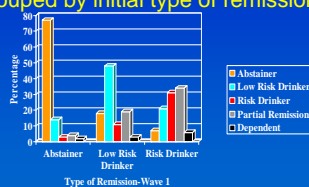
Miller et al., J Stud Alc 62:211-220, 2001

12 Month Treatment Outcomes: Partial Remission Among Drinkers



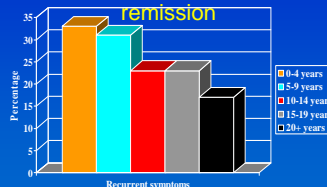
Miller et al., J Stud Alc 62:211-220, 2001

Status of sample after 3 years, grouped by initial type of remission



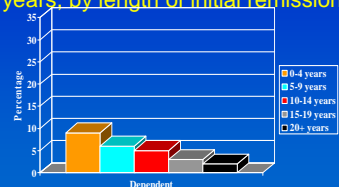
Dawson et al., ACER, 2007

Recurrence of any symptoms after 3 years, by length of initial remission

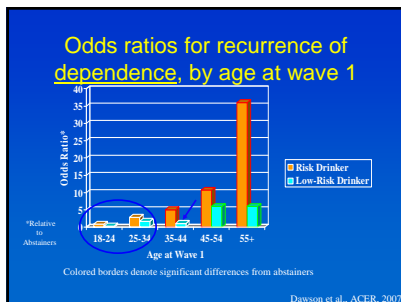
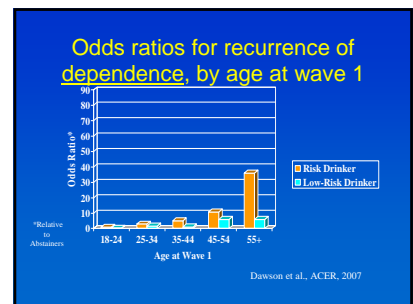
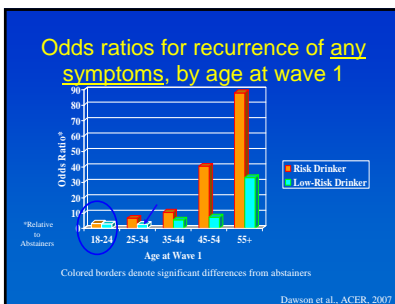
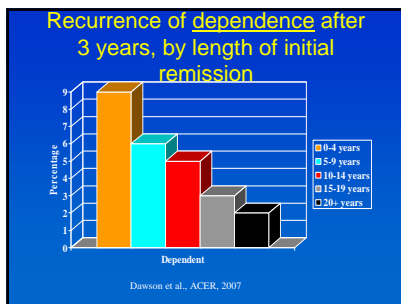


Dawson et al., ACER, 2007

Recurrence of dependence after 3 years, by length of initial remission

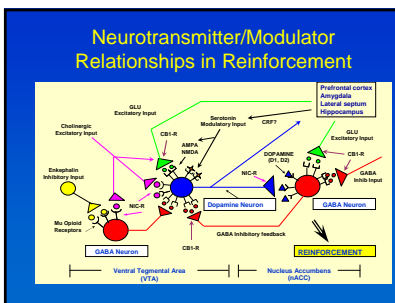
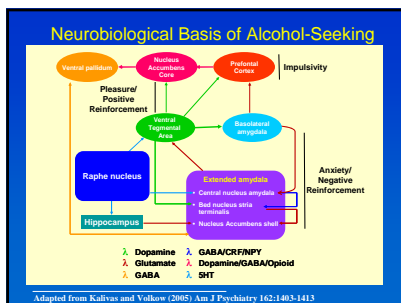


Dawson et al., ACER, 2007



- Notes for interpretation of Dawson et al., ACER, 2007
- This is a community sample, not a treatment population. Thus, these findings do not generalize to treatment seekers.
 - Treatment seekers have more severe dependence, more mental and physical comorbidities, and less social support
 - Thus, for treatment seekers with dependence, abstinence remains the best advice

- Medication treatment for addiction
- Alcohol dependence
 - Disulfiram (Antabuse)
 - Naltrexone (oral, injectable monthly)
 - Acamprosate (Campral)
 - Topiramate (Topamax)
 - Heroin, pain killers
 - Buprenorphine
 - Methadone



- Pharmacotherapy for AD: potentially involved neural systems
- Noradrenergic
 - Serotonergic
 - Opioidergic
 - GABA/Glutamate
 - Endocannabinoid
 - CRF
 - NK-1
 - NPY

Medications to treat alcohol dependence

- Disulfiram (Antabuse)
 - Blocks metabolism of alcohol
 - Causes unpleasant reaction if drinking occurs
 - Useful if patient willing & has adequate judgment
 - Must be monitored administration

Medications to treat alcohol dependence

- Naltrexone (oral generic, Vivitrol for injection)
 - Blocks opioid receptors
 - Reduces reward of drinking
 - Effective in non-comorbid patients
 - May be helpful in reducing drinking in those not committed to abstinence
 - Evidence for efficacy in schizophrenia

Medications to treat alcohol dependence

- Acamprosate (Campral)
 - Acts on GABA-glutamate system
 - Two negative US trials
 - Well tolerated, few interactions
 - Patient must be fully withdrawn and focused on abstinence

Future medication candidates

- Newer antipsychotics
 - Clozapine
 - Quetiapine
 - Ziprasidone
- Anticonvulsants
 - Topiramate
 - Lamotrigine
 - Divalproex

Future medication candidates

- Endocannabinoid antagonists-rimonabant
- CRF antagonists-antalarmin
- NK-1 agonists
- NPY agonists

Medications for opioid dependence

- Opioid agonist therapy is the only treatment proven to reduce morbidity and mortality in heroin dependence
- Buprenorphine (Suboxone/Subutex)
- Methadone
- Works best when combined with skillful behavioral treatment (hard to come by)

Medications for other disorders

- No effective medication treatments currently available for:
 - Cannabis
 - Cocaine
 - Methamphetamine

Summary

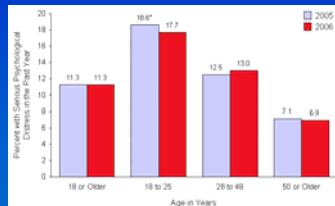
- Intoxicants stimulate the reward centers of the brain, mimicking survival benefit
- The organism adapts to frequent use
- Addiction is characterized by
 - Dysregulation of the hedonic regulatory system
 - Imbalance between the impulsive & reflective brain systems

Summary

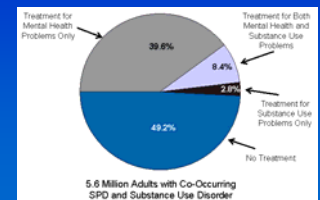
- Most intoxicant use occurs < age 30
- Most users do not develop dependence
- Spontaneous remission is common, but chronicity develops in a significant minority of users
- Genetics account for about 50% of risk
- Treatment effectiveness is similar to that of other common complex diseases

Co-morbidity and SUDs

Serious Psychological Distress in the Past Year among Adults Aged 18+



Past Year Treatment among Adults 18+ with Serious Psychological Distress and SUD: 2006



Co-morbidity clusters in subgroup

Other disorder	Controlled for sociodemographics	+ Controlled for psychopathology
Other drug dependence	18.7*	7.5
Any Mood	3.2	1.7
Any Anxiety	2.7	1.5
Any Personality	3.2	1.8

Hasin et al., Arch Gen Psychiatry 2007 *Odds ratios

What is the relationship?

- Mental disorders in childhood predict adolescent substance use & AUD
 - Conduct disorder & ODD
 - ADHD
 - Mood and anxiety disorders
 - "psychological dysregulation" (Clark, 2005)
 - "behavioral undercontrol" (Sher, 2007)

Complex interaction

- Having more than one disorder makes it more difficult to recover from either
- No simple "self-treatment" paradigm
- Unlikely that mental disorders, in contrast to psychological symptoms, result from alcohol dependence
- People with multiple disorders more likely to present for treatment & have difficulty recovering

Common & specific genetic factors for alcohol dependence

- Common genetic factors (.35)
 - Externalizing disorders
 - Anxiety
- Specific genetic factors (.14)
- Specific environmental factors (.36)

Kendler et al., Arch Gen Psychiatry 2003

National Epidemiologic Survey on Alcohol and Related Conditions 2001 - 2002



- N= 43,093.
- Nationally-representative survey.
- Response rate: 81%.
- Oversampling of Blacks, Hispanics/ Latinos, young adults.
- Longitudinal: second wave fielded July 2004.
- DSM-IV based diagnoses of substance use, mood, anxiety and personality disorders.

Co-Occurrence of Current (12-month) DSM-IV Alcohol Dependence and Other Disorders, Controlled for Sociodemographics and Other Disorders

Disorder	Alcohol Dependence
Any Drug Disorder	5.0 x
Any Mood Disorder	1.7 x
Any Anxiety Disorder	1.5 x
Any Personality D/O	1.8 x

Hasin et al., Arch Gen Psychiatry, 2007

Co-Occurrence of Current (12-month) DSM-IV Alcohol Dependence and Other Disorders, Controlled for Sociodemographics and Other Disorders

Disorder	Sociodemo only	Sociodemo & Other d/o
Drug Dependence	18.7	7.5 x
Any Mood Disorder	3.2	1.7 x
Any Anxiety Disorder	2.7	1.5 x
Any Personality D/O	3.2	1.8 x

Hasin et al., Arch Gen Psychiatry, 2007

Twelve-month Treatment Rates for DSM-IV Alcohol and Any Drug Abuse and Dependence 1991-1992 and 2002-2002

	1991-1992*	2001-2002
Alcohol Abuse	4.4%	3.1%
Alcohol Dependence	13.8%	12.1%
Any Drug Abuse	4.1%	6.1%
Any Drug Dependence	19.5%	30.7%

* 1991-1992 rates based on NIAAA's National Longitudinal Alcohol Epidemiologic Survey (NLAES).

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2000-2001.

The Extent of Comorbidity Among Respondents with DSM-IV Alcohol Use Disorders in the General Population and Among Those in Treatment for These Disorders - Past 12 Months

# of Other Psychiatric Disorders	General Population	Treatment
0	40.9%	21.3%
1	26.8%	18.7%
2	14.2%	17.9%
3	7.2%	11.3%
4-5	6.7%	17.0%
6+	4.2%	13.7%

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2000-2001.

The Extent of Comorbidity Among Respondents with DSM-IV Alcohol and Drug Use Disorders in the General Population and Among Those in Treatment for These Disorders - Past 12 Months

# of Other Psychiatric Disorders	General Population	Treatment
0	14.5%	4.9%
1	21.7%	14.2%
2	22.2%	14.5%
3	12.2%	15.9%
4-5	16.6%	27.4%
6+	12.9%	23.1%

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2000-2001.

Significant Co-Occurrence of Current (12-month) DSM-IV Alcohol Dependence (after controlling for sociodemographics and other disorders)

Disorder	Alcohol Dependence
Bipolar disorder	2.0 x
Histrionic/ASPD	1.8 x

Hasin et al., Arch Gen Psychiatry, 2007

SUD, psychosis and BPAD

	SczAff-BP	BPAD	Scz
Alcohol*	53%	60%	31%
Other drug*	74%	68%	36%
FHx Mood*	66%	79%	33%

*p<0.01. Five-year retrospective study

Nardi et al., J Affect Dis 2005

Days of medication use

	SczAff-BP	BPAD	Scz
Antidepr*	815	714	158
Mood Stab*	1098	1460	388
Antipsych*	927	862	1655

*p<0.05. Five-year retrospective study

Nardi et al., J Affect Dis 2005

Medications: what doesn't reduce drinking in co-morbid patients?

- Antidepressants
- Lithium
- Traditional antipsychotics
- Benzodiazepines

What does reduce drinking?

- Divalproate in bipolar/AD
- Naltrexone in schizophrenia
- Clozapine in schizophrenia (probable)

