

SUBSTANCE ABUSE: Pharmacology & Neurology (p.1)

1. Historical Perspective

every society has used drugs to --- effect change in mood, thought, behavior, to *temporarily* change perception of reality

and in every society some individuals **abused** these drugs meaning that they used the drug(s) outside of the society's sanctioned uses (time, place, amount, etc.)

and these unsanctioned users always --- **problems** for self, for those around them, for the greater society

traditionally, these abusers only used a **small # of drugs** that each society had access to...which helped to keep **small the number of abusers**

but not now!

there are many psychoactive drugs available now

there is **fairly easy access** to these **many drugs**

there are many **synthetic derivatives** available...and more coming every day... “designer chemistry” available to all via internet

there are new drug delivery techniques (e.g. alkaloid salts of drugs to be smoked)

some drugs are now **inexpensive, available and socially sanctioned!**

2. Concerning Drug Abuse Treatments

treatment costs a lot...but not treating costs a lot more!

substance abusers are heterogeneous in nature/severity of abuse thus, one treatment approach will not fit all abusers

majority of abusers have comorbid (dual) psychiatric diagnoses that must also be treated

SUBSTANCE ABUSE: Pharmacology & Neurology (p.2)

2. Concerning Drug Abuse Treatments (cont.)

in some cases, the psychiatric Dx's have --- to drug abuse ("self-medication")

in some cases, the drug abuse has --- psychiatric symptoms or both!

multiple factors **sustain drug abuse patterns:**

reinforcing effects of drug

"permanent" or treatment resistant changes in NS

avoidance of withdrawal effects

a beneficial decrease in underlying psychiatric symptoms

social reinforcement for drug use

financial gain

drug use often starts very early in life, lifestyle difficult to change

drug use decreases awareness of aversive elements in abuser's life

lack of treatment options, lack of access to treatment

other

3. Nosology & Epidemiology of Substance Dependence/Abuse

see DSM IV, Table 13.1, p. 370

substance **abuse** --- leads to substance **dependence**

maladaptive patterns of substance use --- to significant impairment & distress

1 or more = abuse

role failure

dangerous to self/others

legal problems

continued used despite problems

3 or more = dependence

tolerance

dependence & w/d Sxs

increasing amounts, duration of use

cannot decrease use, more efforts to obtain drug

loss of + roles, replaced by drug use

use continues while S acknowledges problems

SUBSTANCE ABUSE: Pharmacology & Neurology (p.3)

Epidemiology:

“**prevalence**” = highest # of cases in entire population

e.g. **alcohol** is drug with highest prevalence of all psychoactive drugs

“**lifetime prevalence**” of alcohol is 13-23% of population of USA
(vs. 6% mean average for all other psych.act. drugs)

current data on young adults (late teens to early 20's) on “**have ever used**”:

90% alcohol	14% inhalants (e.g. gasoline)
65% nicotine (smoked)	14% stimulants
53% marijuana	12% cocaine
25% nicotine (chewed)	9% opiates
16% hallucinogens (not MJ)	

about **33% of Ss** with drug addictions also have a **comorbid psych. diagnosis**

of drug abuse/dependent Ss:

60% “personality disorders”

50% “bipolar”

47% “schizophrenic/schizoid”

33% “OCD”

30% “unipolar depression” (males = females)

24% “anxiety”

Julien argues that both substance abuse/dependence and psychiatric diagnosis must be treated concomitantly

Preston argues that substance abuse/dependence must be treated first; that drug abstinence is necessary before one can treat psych diagnosis

what do you think?

SUBSTANCE ABUSE: Pharmacology & Neurology (p.4)

4. Psychoactive Substances as Behavioral Reinforcers

What is the biochemistry, neurophysiology, and neuropathology of behavioral reward as it pertains to substance abuse/dependency?

substances that are prone to compulsive abuse activate the reward (positive reinforcement/attentional focus) areas of the CNS:

medial forebrain bundle

ventral tegmentum

hippocampus

frontal cortex (orbital/basal prefrontal)

nucleus Accumbens

mesocorticolimbic pathway

amygdala

and they tend to be **agonists for: DA (esp. DA2), 5HT, opioid, GABA, and cannabinoid RSs** (maybe NE...)

note: cocaine seems to be the “mother” of all reinforcers; all animal species so far tested (N=8) will self-administer it

a “loop” of fibers: DA
basal forebrain (prefrontal cortex) ventral tegmentum of
& nucleus Accumbens, midbrain
amygdala, septal area
opioids, DA, GABA, 5HT & NE
medial forebrain bundle

note: Ss who are **DA2 RS deficient** are more likely to show drug abuse/dependence, more likely to abuse methylphenicate/Ritalin and find it pleasurable, and are more likely to use cocaine

How does S become DA2 RS deficient? inherited? acquired? congenital?

SUBSTANCE ABUSE: Pharmacology & Neurology (p.5)

4. Behavioral Reinforcers (cont.)

the 3 major factors that maintain drug abuse/dependence are:

neural mechanisms

e.g. DA2 RS deficiencies; too much activity in reward/focus “go for it” areas in CNS;
activity in hypothal-pituitary-adrenal axis (such as increases in cortisol seen in depression, which may --- sub.abuse/depend);
underactivity in prefrontal “do not do this” areas of brain

behavioral mechanisms

impaired because of depression, anxiety
avoidance of adverse withdrawal effects
seeking of feelings of well-being, euphoria

modifying factors

social context of drug use (all my friends do it too, it is “cool”, vs. it is not acceptable in my group of associates)

genetic factors account for about 1/3 of variance of overall drug use

attitudes & expectations (cognitive factors) in self, others

previous history

drug availability

which has been the major emphasis to date in attempting to control drug use...and has **not** been very successful

also, legislation has failed to address impact of **legally sanctioned** & available drugs on sub. abuse/dependency (ETOH, nicotine, caffeine)

most likely making currently illegal drugs legal to obtain would **not** help reduce sub.abuse/dependency, although it might **reduce criminal acts** associated with obtaining drugs

SUBSTANCE ABUSE: Pharmacology & Neurology (p.6)

5. Drug Education

to be effective, it must have 3 elements:

basic information

means for behavioral change

e.g. how to resist peer pressure

methods for **reinforcing new (non-drug) behaviors**

e.g. play baseball vs. take drugs

increase S's **self-esteem** in a drug-free environment

requires adults to be good non-drug using **role models** for child

must be **consistent** re. the harm of drug use, incl. alcohol, nicotine,
(and caffeine?) (and marijuana?)

6. Treatment Issues

out-moded idea – that sub.abuse/dep. was maintained simply by the S's
avoidance of adverse effects of w/d

used to think that treatment = detoxification, with the assumption that
once S was through w/d and totally abstinent, that S was now OK
and would not relapse back to drug use...**wrong!**

by mid-1990s we faced the fact that most former drug abusers return to
drug use, do relapse....necessitated a change of focus in tx

recognition that in **abstinence** state former user feels **not-normal:**

apathetic, bored, depressed, anhedonic, malaise, anxious, depressed
& **craves** relief from this state (which he sees possible only by
using drug X)

when **S uses drug X**, he/she feels **more normal:**

more energy, less depressed, can enjoy things, motivated
but...may not be able to work, engages in criminal behavior in
order to obtain drug X, suffers social/familial stigma, feels a
“failure”, is alienated from others, etc. – a big price to pay!

SUBSTANCE ABUSE: Pharmacology & Neurology (p.7)

7. Pharmacological Treatment

use pharmacological treatments **plus** behavioral treatments,
both are necessary
in particular, how to handle exposure to **drug-using trigger cues**
& **drug-craving trigger cues**

pharmacological:

initially treat **to reduce adverse withdrawal Sxs**

may **substitute a legally obtained drug** (e.g. methadone)
usually substitute drug has a longer $\frac{1}{2}$ life (reduces w/d Sxs)
eliminates the criminal element from obtaining the drug

may substitute legally obtained drug for **long-term maintenance**
note: goal is not longer for abstinence per se

may use a **drug RS antagonist** (esp. DA2 or opiate) to reduce drug
cravings (which seem to be related to a signal from unoccupied RSs)

treatment of comorbid psychological disorder with non-addicting,
legally obtained medications

overall pharmacological goals are to:
decrease intensity of withdrawal Sxs
decrease rate of relapse

each addictive drug is treated with specific drugs:

opioid abuse/dependence –

substitute longer-acting legally obtained opiate agonist

Methadone, LAAM (l-alpha-acetylmethadone)

clonidine (NE alpha agonist)

w/ or w/o naltrexone (opiate antagonist)

RAAD – expensive and controversial, riskier, high relapse rate

SUBSTANCE ABUSE: Pharmacology & Neurology (p.8)

7. Pharmacological Treatment (cont.)

opioid abuse/dependence – (cont.)

for **maintenance approach** use **opiate agonists/partial agonists**

methadone, LAAM, buprenorphine (Buprenex)

or use opiate antagonists, naltrexone (Trexan, ReVia)

usually poor patient compliance

nicotine abuse/dependence –

nicotine replacement tx that does not require smoking per se

gums, patches, nasal sprays, inhalers

antidepressants

esp. bupropion (Wellbutrin, Zyban)

works as an antidepressant and decreases cravings (inhibits DA reuptake)

above are all maintenance approaches, not abstinence

ETOH abuse/dependence –

tx for w/d (detox), aversive therapy, decrease cravings, comorbid Dx's

detoxification – decrease alcohol, increase BZDs (e.g. Librium,

Valium, Klonopin) long ½ lives

decrease risk of seizure, decrease w/d Sxs (e.g. anxiety, insomnia)

Antabuse (disulfiram) for **aversive th.**

to **decrease cravings** – naltrexone (blocks opiate RSs)

acamprosate () – glutamate antagonist, used in Europe

ibogaine (a Schedule I “narcotic”), decreases cravings, structurally

similar to 5HT (in rats it decreases consumption of ETOH,

morphine & cocaine)

is a DA antagonist via effects on 5HT, kappa opiate, & glutamate RSs

...but has psychedelic properties, which are undesirable

to **treat depression** – SSRIs, other antidepressants (common comorbid disorder, also anxiety)

SUBSTANCE ABUSE: Pharmacology & Neurology (p.9)

8. Behavioral Treatment

(see p.382, Figure 13.6, Julien, 9th ed.)

regular **outpatient** treatment program attendance

is the most cost-effective approach after detox. has been completed

44% abstinent at 1 year anniversary for detox + outpatient

\$1500 for just detox (**34%** abstinent at 1 year anniversary)

sometimes done **inpatient** as well, but more costly (\$7000 vs. \$1500)

but patient is there! so is slightly more effective than outpatient

(when patient is not always there!) (**50%** abstinent at 1 year)

note: cost of 1 year in jail = \$26,000

note: even brief behavioral counseling (5-10 minutes) is more effective than no behavioral counseling at all...

treatment issues:

discuss and acknowledge positive and negative aspects of drug use, and the ambivalence...

teach coping skills – for trigger avoidance especially

changing reinforcers to non-drug ones

managing painful, negative effects of abstinence, from other sources in a non-drug way

improve interpersonal skills, enlarge social support network

improve compliance with pharmacotherapy

