Drugs

Still chapter 4!
Drug Classification

• There is no generally agreed-upon classification of psychoactive drugs.

• So this one will have to do.
Dr. King’s Drug Classification Scheme for Psychoactive Drugs

• others (hard to classify!) - nicotine, marijuana, PCP, etc.
• stimulants - caffeine, amphetamines, methylphenidate, cocaine, etc.
• depressants / sedatives / tranquilizers / anxiolytics - alcohol, barbiturates, benzodiazepines, etc.
• opiates (these are the drugs pharmacologically known as narcotics) - opium, morphine, heroin, etc.
• psychedelics / hallucinogens / psychotomimetics - LSD, mescaline, psilocybin, DMT, etc.
• psychotherapeutics
  • antidepressants - MAOIs, tricyclics, SSRIs, etc
  • antipsychotics - chlorpromazine, haloperidol, clozapine, etc.
A Quick Simpleminded Rundown of What They Do in the Brain

- others (hard to classify!) - various actions
- stimulants - catecholamine agonists (mostly)
- depressants / sedatives / tranquilizers / anxiolytics - GABA agonists (mostly)
- opiates (narcotics) - endorphin agonists
- psychedelics / hallucinogens / psychomimetics - various actions on serotonin
- psychotherapeutics
  - antidepressants - monoamine agonists (mostly)
  - antipsychotics - dopamine antagonists
Dependence Potential

- Dependence has more to do with craving than with withdrawal avoidance.
- Dependence potential often depends on how the drug is taken and for what reasons.
- Dependence means a user has lost control of his/her intake of the drug (denial aside!).
- based on Gable (1993)
Dependence Potential

- high to very high dependence potential
  - heroin (IV)
  - crack cocaine
  - morphine (injected)
  - opium (smoked)
Dependence Potential

- moderate to high/moderate
- cocaine (snorted)
- tobacco (smoked)
- PCP (smoked)
- Valium
- alcohol
- amphetamines (oral)
Dependence Potential

- low to low/moderate caffeine
- MDMA (ecstasy)
- marijuana
- LSD, mescaline, psilocybin
What Are “Schedules” (A Legal Construct)

• Schedule I - high abuse potential, no recognized medical use (in U.S.)
  • heroin, marijuana, MDMA

• Schedule II - high abuse potential, currently accepted medical use
  • morphine, cocaine, methamphetamine

• Schedule III - moderate abuse potential, currently recognized medical use
  • anabolic steroids, barbiturates, THC

• Schedule IV and Schedule V
Nicotine (Tobacco)

• Tobacco smoking was discovered among the inhabitants of the “New World” by Columbus.

• The first person to be observed smoking tobacco in Europe was imprisoned, because it was believed he was possessed by the devil.

• By the mid-1500s, “medical uses” had been found for tobacco, which legitimized its use.
Nicotine (cont.)

- Nicotine was first isolated from tobacco in 1828 by two French chemists.
Nicotine (cont.)

• Nicotine was finally recognized in the U.S. to have no medical use in the 1890s.
• It has been used as an insecticide, however. (This use has recently been banned worldwide.)
• It is very toxic and very fast-acting. A cigar contains about two lethal doses!
  • low level poisoning - dizziness, nausea
  • acute poisoning - tremors, convulsions, death (from paralysis of the respiratory muscles)
• “Back in the lab,” nicotine was the drug we least liked to handle.
Nicotine (cont.)

- Nicotine occupies and activates the nicotinic acetylcholine receptor.
- However, it does not release from the receptor very quickly, so it also has a short blockade effect.
- Stimulates the release of adrenalin from the adrenal gland.
- Shifts the cortical EEG to an activated pattern.
Nicotine (cont.)

• Nicotine affects the appetite in two ways.
  • inhibits hunger pangs (stomach contractions)
  • deadens the taste buds

• Nicotine withdrawal results in increased appetite, probably due to a return of taste sensitivity.

• (The old Freudian pearl that it has to do with deficient oral gratification is, to be polite, bulls**t!)
Nicotine (concluded)

- Tolerance develops rapidly.
  - This is probably due to induction of liver enzymes that break it down.
- Nicotine is highly addictive.
  - This is probably because it activates the mesolimbic dopamine pathway that terminates in the nucleus accumbens in the ventral basal ganglia.
Caffeine

- Caffeine and its relatives, theophylline and theobromine, are chemically known as xanthines.
- It is the most commonly used psychoactive substance in existence.
- 80% of Americans use it on a daily basis.
Caffeine (cont.)

• Most modern kitchens have a device specially designed for the extraction of caffeine from plant material. It’s called a coffeemaker.

• Other sources of caffeine: tea, colas, chocolate, cocoa, “energy” drinks (which contain less caffeine that a cup of coffee!), OTC “pep” pills and diet pills

• Aside: caffeine that is removed from decaf coffee is often added to colas.
## Caffeine (cont.)

<table>
<thead>
<tr>
<th>Item</th>
<th>Amount</th>
<th>Caffeine (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk chocolate</td>
<td>8 oz</td>
<td>5</td>
</tr>
<tr>
<td>Dark semi-sweet chocolate</td>
<td>1 oz</td>
<td>20</td>
</tr>
<tr>
<td>Brewed green tea</td>
<td>8 oz</td>
<td>20</td>
</tr>
<tr>
<td>Anacin</td>
<td>one tablet</td>
<td>32</td>
</tr>
<tr>
<td>Pepsi cola</td>
<td>12 oz can</td>
<td>38</td>
</tr>
<tr>
<td>Espresso</td>
<td>1 oz shot</td>
<td>40</td>
</tr>
<tr>
<td>Fiorinal/Fioricet</td>
<td>one tablet</td>
<td>40</td>
</tr>
<tr>
<td>Coca-cola</td>
<td>12 oz can</td>
<td>46</td>
</tr>
<tr>
<td>Brewed black tea</td>
<td>8 oz</td>
<td>50</td>
</tr>
<tr>
<td>Mountain Dew</td>
<td>12 oz can</td>
<td>54</td>
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<tr>
<td>Midol</td>
<td>1 gelcap</td>
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</tr>
<tr>
<td>Excedrin pain reliever</td>
<td>1 tablet</td>
<td>65</td>
</tr>
<tr>
<td>Dexamethasone Natural</td>
<td>one tablet</td>
<td>80</td>
</tr>
<tr>
<td>Jolt cola</td>
<td>12 oz can</td>
<td>80</td>
</tr>
<tr>
<td>Red Bull energy drink</td>
<td>8.3 oz can</td>
<td>80</td>
</tr>
<tr>
<td>Monster energy drink</td>
<td>16 oz can</td>
<td>80</td>
</tr>
<tr>
<td>Jolt caffeine energy gum</td>
<td>2 pieces</td>
<td>100</td>
</tr>
<tr>
<td>Penguin caffeinated mints</td>
<td>6 pieces</td>
<td>100</td>
</tr>
<tr>
<td>Cafegrot</td>
<td>one tablet</td>
<td>100</td>
</tr>
<tr>
<td>No Doz</td>
<td>one tablet</td>
<td>100</td>
</tr>
<tr>
<td>Brewed coffee</td>
<td>12 oz cup</td>
<td>200</td>
</tr>
<tr>
<td>Vivarin</td>
<td>one tablet</td>
<td>200</td>
</tr>
<tr>
<td>Ripped Fuel Extreme Ephedra Free</td>
<td>2 capsules</td>
<td>220</td>
</tr>
</tbody>
</table>
Caffeine (cont.)

• Caffeine was first isolated from coffee in 1820.

• Caffeine is taken up fairly rapidly, reaches its maximal pharmacological effect in the CNS in about 2 hours, and has a half life of about 3 hours in the human body.

• Tolerance develops rapidly and is long-lasting.

• Both psychological and physical dependence occur. The most reliable withdrawal symptoms are headache (within 24 hrs.), fatigue, and lassitude. Withdrawal takes about a week.
• At one time it was believed that the action of caffeine was on the second messenger system at catecholamine neurons.

• Today we think the primary action is blockade of adenosine receptors.

• Causes cortical arousal and activation of the EEG.

adenosine - promotes sleep and suppresses arousal; builds up in the brain during wakefulness
Caffeine (concluded)

- behavioral/psychological effects
  - stimulation, arousal, elevation of mood
  - relief from fatigue
  - relief of headache (withdrawal can produce headaches and lead to the onset of migraines)
  - precipitation of panic attacks in people prone to them (at a dose equivalent to about 5 cups of coffee)
  - there is no evidence that caffeine (or coffee) will help you “sober up”
Amphetamines

- All amphetamines are variants of this structure.
- Adding methyl groups to it makes it more easily cross the blood-brain barrier.
- Adding hydroxyl groups to it makes it less easily cross the blood-brain barrier.
Amphetamines (cont.)

- Ephedrine is an amphetamine.
- Methamphetamine is an amphetamine.
- Methylphenidate (Ritalin) is NOT an amphetamine.
  - Although it is commonly called one and has similar effects.
  - There is an “amphetamine-like” part to the molecule.
Amphetamines (cont.)

- Amphetamines were first known by the Chinese and were used in herbal form. We call the herb Ephedra.
- Ephedrine, the active compound in Ephedra, has largely “sympathomimetic” effects.
  - nasal and bronchial dilation
  - elevated blood pressure
- Knowledge of ephedrine led to the synthesis and investigation of similar compounds.
Amphetamines (cont.)

- Amphetamine was first synthesized in the 1920s and patented in 1932 as Benzedrine.
- It was first used in the treatment of asthma, and later in the treatment of narcolepsy.
- It also became used as an appetite suppressant and to treat hyperactivity in children.
- “Bennies” became a favorite of long haul truckers to help keep them awake and of college students who had to cram for exams.
Amphetamines (cont.)

• In the 1950s and 1960s it became widely and easily available as a prescription treatment for depression and obesity.

• In the 1960s, amphetamines became among the most popular drugs of abuse and became known as “speed” (a name previously applied to cocaine), especially when used IV.

• In 1965 amphetamines were labelled dangerous by the Federal government and became restricted. In the public’s mind, use of the drug became associated with “drug-abusing hippies.”
Amphetamines (cont.)

• There were three consequences.
  • The “hippies” began to lose interest in this synthetic drug and took up use of a “more natural” plant-derived stimulant - cocaine.
  • By 1980 if you were buying “speed” on the street, you were almost surely getting a look-alike pill containing caffeine, ephedrine, and other legal substances.
  • Illegal meth labs became much more common.
Amphetamines (cont.)

• The chemical structure is very similar to that of the catecholamine neurotransmitters.

• Apparently, amphetamines are “mistaken” for catecholamines in the brain.

• d-Amphetamine (Dexedrine) is several times more potent in the CNS than l-amphetamine.

• Amphetamines stimulate the release of all the monoamine neurotransmitters.
Amphetamines (cont.)

• The euphoria (“rush”) associated with amphetamine use is commonly attributed to its ability to release DA in the nucleus accumbens (mesolimbic DA pathway).

• However, specific DA antagonists do not block this effect of amphetamine.

• High doses are so good at dumping MA neurotransmitters that depletion can occur, leading to a “crash.”
Amphetamines (concluded)

- problems
- impaired decision making
- possible increase in violent behavior (??)
- amphetamine psychosis
- compulsive, stereotyped behavior
- neurotoxicity after high doses
- craving, lethargy, and depression upon withdrawal
Cocaine

- Cocaine is derived from the leaves of Erythroxylon coca, the cocoa (coca) plant.
- This plant has been cultivated by South American Indians for 7000 years.
Cocaine (cont.)

- It was introduced to Europeans as coca wine in the late 19th century.
Cocaine (cont.)

• ...and to Americans as Coca Cola.

• The name was derived from the source of the two stimulants it contained: cocoa leaves and cola beans.
Cocaine (cont.)

- It’s first medical use was as a local anesthetic.
- It was replaced eventually by procaine (Novocain).
Cocaine (cont.)

- It was also used in the treatment of depression and morphine dependency.
- These uses were endorsed by Sigmund Freud.
Cocaine (cont.)

- Like nicotine, its chemical structure is not very revealing of what it might do in the brain.
Cocaine (cont.)

- two forms
  - cocaine hydrochloride
    - so stable it does not form vapors when heated - so can’t be smoked
    - dissolves in water, so can be snorted
  - cocaine freebase (crack) - forms vapors when heated
Cocaine (cont.)

• Cocaine is broken down in the liver. It has about a 1-hour half life.

• Cocaine is a powerful stimulant.
  • arousal/activation
  • relieves fatigue
  • reduces appetite
Cocaine (cont.)

- acute cocaine poisoning - from high doses
  - convulsions
  - respiratory arrest
  - cardiac arrest
- cocaine psychosis - similar to amphetamine psychosis
- Lab animals allowed to self-administer cocaine will do so until they die.
Cocaine (concluded)

• Physical withdrawal may not occur.
• Craving, irritability, and depression are common upon withdrawal.
• The “crack baby” phenomenon was mostly hype. Although it is well known that what a mother takes while she is pregnant can influence the development of the fetal brain. This has been shown in animal experiments with drugs like barbiturates and benzodiazepines.
Barbiturates

- Barbiturates are sedative drugs based on the barbituric acid molecule.

- They have some of the most colorful street names: reds, red birds, red devils, blues, blue heavens, yellows, yellow jackets, tooties, and goofballs.
Barbiturates (cont.)

- “downers”
  - sedatives - tranquilizers or anxiolytics
  - hypnotics - sleeping pills
- as opposed to “uppers” - stimulants
- Similar depressant effects are produced by alcohol and inhalants (glues, paints, solvents).
- Once among the most frequently prescribed drugs, today they have been largely replaced by the benzodiazepines (Librium, Valium, Xanax, etc.).
Barbiturates (cont.)

- Barbiturates were introduced to clinical use in 1903. (Marketed by Bayer as a hypnotic and anesthetic. They were also used as anticonvulsants.)

- They are classified as “short-acting” (15 min. onset, 2-3 hrs. duration), “intermediate-acting”, and “long-acting” (1 hr. onset, 6-10 hrs. duration). Now what do you think this could be related to??? :-)

- There are ultra-short acting barbiturates that will put you to sleep within a minute of IV injection.
Barbiturates (cont.)

• Tolerance develops rapidly due to induction of liver enzymes.

• They depress respiration and in high doses or in combination with alcohol can cause respiratory arrest.

• In the 1950s and 1960s, they were the drugs of choice for committing suicide. An “overdose of sleeping pills” meant suicide by barbiturates.

• Today they are used to euthanize animals, in physician assisted suicide, and in capital punishment by lethal injection.

• Sodium Pentothal, or “truth serum,” is also a barbiturate. (It doesn’t really make you tell the truth!)
Barbiturates (cont.)

• Barbiturates do cross the placental barrier, so women taking them while pregnant can give birth to barbiturate-addicted babies.

• withdrawal - characterized by the opposite effects of the drug itself
  • dysphoria
  • anxiety, hyperventilation, panic attacks
  • insomnia
  • seizures
Barbiturates (concluded)

- Barbiturates act at a barbiturate binding site on the GABA-A receptor, where they cause the chloride channel to remain open longer.

- The endogenous ligand is unknown.

- They may also have a secondary action of blocking AMPA receptors.
Some Other Sedatives

• “Mickey Finn” or knock-out drops - chloral hydrate (takes effect in about 30 min.; puts you to sleep in about an hour, unlike in the movies!)

• Methaqualone - sold under trade names Quaalude and Sopor

• benzodiazepines - Librium, Valium, Xanax, Ativan, Halcion, and about 50 others

• Rohypnol (“roofies”) - a benzodiazepine sometimes used as a “date rape” drug (now changes color when added to alcohol!)

• GHB - gamma-hydroxybutyrate (a GABA-like chemical)

• Ambien/Lunesta/Sonata - have a benzodiazepine-like action at the GABA receptor
Answers to Questions

- euthanizing a pet (small animals)
  - may be done in one or two injections
- sodium pentobarbital (Nembutal) is used
- tranquilizer guns - typically not barbiturates (why not?)
  - opiates - fentanyl, etc.
  - heavy duty antipsychotics like haloperidol
  - ultra-short-acting benzodiazepines
  - paralytics like curare
  - “cocktails” of the above

- death penalty by lethal injection
  - a three-stage process
  - sodium thiopental - an ultra-short-acting barbiturate
  - pancuronium - a paralytic that stops breathing (a curare-like drug)
  - potassium chloride - stops the heart
Morphine and Heroin

- These drugs are either derived from the opium poppy (Papaver somniferum) or are synthetic work-alikes.

- Opium has been known and used medically for at least 6000 years.
M & H (cont.)

- Morphine was first isolated from opium in 1806, and is the primary active ingredient in opium. (Codeine was isolated in 1832.)
- The first widespread use of morphine was in the American Civil War for relief from pain and treatment of dysentery.
  - Morphine addiction was for a time called “the soldiers’ disease.”
- Heroin (diacetylmorphine) was first marketed by Bayer in 1898 (as a non-habit-forming replacement for codeine).
M & H (cont.)

• Heroin enters the brain faster than morphine. Why? (~3X as potent)

• Once in the brain, heroin is converted to morphine. So for all intents and purposes, they are the same drug.

morphine

heroin
M & H (cont.)

- patent medicines

  - for asthma
  - for teething pain
  - for coughs
  - for “fretfulness”
In the 1880s the typical users of opium in this country were middle-aged housewives who may have ordered their opium from the Sears-Roebuck catalog.
Today there is a large number of synthetic opiates. They all work the same way.

- meperidine (Demerol)
- oxycodone (Percodan, Oxycontin)
- hydrocodone (Vicodin)
- propoxyphene (Darvon)
- fentanyl (Sublimaze)
M & H (cont.)

• For decades everybody believed there was an opiate receptor in the brain.

• It was discovered in the 1970s.

• We had to ask, “Why the heck is that there?”

• The endogenous ligands (the endorphins or “endogenous morphines”) were discovered in 1974.
• leu-enkephalin, met-enkephalin
• endorphins
• dynorphins
• They all act at one of another type of opioid receptor in the brain.
• Endorphins are also released from the pituitary gland in response to stress.
• Enkephalins are released from the adrenal gland.
M & H (cont.)

• As pain relievers, these drugs seem to work primarily on the emotional component of pain (suffering), and only secondarily on the sensation of pain.

• They are also used for the treatment of intestinal disorders, diarrhea, and as cough suppressants.

• They are abused because of their potential to create euphoria.

• There is NO credible evidence that naturally occurring opioids produce euphoria. (“Runner’s high,” if it exists at all, is not due to an action of endorphins!)
M & H (cont.)

- Tolerance develops to most if not all the effects of opiates, requiring the dose to be increased if used repeatedly.

- Cross-tolerance occurs between all opiates.

- Behavioral tolerance - the effect of opiates used repeatedly is less if they are used in a familiar setting. (This can lead to overdosing in unfamiliar settings.)
M & H (cont.)

• After chronic use of high doses, a characteristic abstinence syndrome occurs when the drug is withheld.
  • 6 hrs: craving, anxiety
  • 12 hrs: yawning, sweating, runny nose, teary eyes
  • 18 hrs: goose bumps, tremors, hot and cold flashes, aching bones and muscles, loss of appetite
  • 24 hrs: increased BP, increased body temperature, increased respiratory rate and depth, nausea
  • 36-48 hrs: vomiting, diarrhea, seizures in those prone to them
M & H (concluded)

• acute toxicity (overdose)
  • respiratory depression - due to the respiratory centers of the medulla becoming less sensitive to carbon dioxide in the blood; this is very much accentuated by alcohol and other sedatives, and most deaths are due to the combination

• pinpoint pupils

• coma

• treated with naloxone - an endorphin receptor blocker
Hallucinogens: An Overview

- **indole hallucinogens** - LSD, lysergic acid amide, DMT, 5-methoxy-DMT, psilocybin
- **catechol hallucinogens** - mescaline (peyote), DOM (STP), MDA, MDMA (ecstasy) [last 3 are amphetamine derivatives]
- **deliriants**
  - PCP, ketamine, dextromethorphan, nitrous oxide
  - anticholinergics - belladonna (atropine, scopolamine), mandrake, henbane, datura
  - amanita muscaria (ibotenic acid, muscimol)
  - salvia divinorum
LSD

• myths

• People on LSD have gone blind from staring into the sun. (Patently false.)

• LSD causes chromosomal damage. (True, but no more so than other drugs.)

• The Beatles song Lucy in the Sky with Diamonds was written about LSD. (It was written about a childhood friend of Julian Lennon’s named Lucy.)
LSD

• truths

• LSD is one of the most potent psychoactive substances known. (True. It becomes active at a dose of about 50 micrograms, or less in some people, about 1/1000 the dose required for most drugs.)

• If you buy mescaline (or other exotic hallucinogens) on the street, you are almost certainly getting LSD.

• LSD is about the most incredibly boring drug to study in rats that you can possibly imagine!
LSD (cont.)

- LSD is one of the least toxic drugs known.
- TI = 400 (in rats)
- no known physical dependence
LSD (cont.)

- Only a very small amount of ingested LSD gets to the brain.
- Half life is about 3 hrs.
- Tolerance develops rapidly after only a few daily doses (and is virtually complete).
- Cross-tolerance occurs with psilocybin and mescaline.
- Effects are blocked by chlorpromazine (Thorazine) and certain other antipsychotics.
LSD (cont.)

- LSD acts at a variety of serotonin receptor subtypes, but it is agonistic at some and antagonistic at others.

- The most specific action of LSD (as well as psilocybin and mescaline) is at the 5-HT\textsubscript{2A} receptor, where it is a direct receptor stimulator.

- (Not all effects are blocked by serotonin receptor blockers, however.)
LSD (cont.)

• the 5-HT$_{2A}$ receptor

• Hallucinogenic effects are highly correlated with a drug's affinity for this receptor.

• Activation of this receptor is necessary for hallucinogenic effects.
LSD (cont.)

- the 5-HT$_{2A}$ receptor (cont.)
  - metabotropic with a complex mechanism
  - located throughout CNS (and body) but especially in the neocortex
  - enhances glutamate release
  - interacts with other NT receptors
It’s now thought that the effects of these classic hallucinations are mediated by 5-HT$_{2A}$ receptors on the apical dendrites of pyramidal cells in layer 5 of the prefrontal cortex.
LSD (concluded)

• Unfortunately, that is where the story seems to end at the present time.

• Prefrontal cortex function is poorly understood except in the most general terms. It has an “executive function” and is important in “cognitive functioning.”

• Schizophrenia, bipolar disorder, and ADHD may be related to malfunctions in prefrontal cortex.

• Clozapine and some other antipsychotic drugs block these receptors.
Cannabis

- various forms of cannabis are derived from the flowering plant *Cannabis sativa*
- marijuana, hashish, and hashish oil
- the first recorded use was in Herodotus’s *Histories* (c.440 BC) - "The Scythians, as I said, take some of this hemp-seed, and, creeping under the felt coverings, throw it upon the red-hot stones; immediately it smokes, and gives out such a vapour as no Grecian vapour-bath can exceed; the Scyths, delighted, shout for joy."

- cannabis was grown in the American colonies for use in rope, clothing, and paper
Cannabis (cont.)

• fourth most popular recreational drug in the world (behind alcohol, caffeine, and tobacco (most commonly used illegal drug)

• primary psychoactive effects: relaxation, minor euphoric effects ("stoned" feeling), increased appetite, impaired short-term memory, poor concentration, impaired motor skills

• withdrawal after everyday use: irritability, insomnia, possibly increased anxiety - usually mild
Cannabis (cont.)

- chronic cannabis use is associated with:
  - impaired short-term memory
  - impaired mental ability in those who started using as teenagers (unclear whether this is permanent)
  - behavioral problems in children whose mothers smoked during pregnancy
  - increased risk of developing schizophrenia in those who start using as teenagers (under investigation; not all researchers are convinced this is a cause-and-effect relationship)
  - neurological changes in brain regions rich in endocannabinoid receptors - hippocampus, prefrontal cortex, amygdala, and cerebellum
Cannabis (cont.)

• the main psychoactive component is delta-9-tetrahydrocannabinol (delta-9-THC)

• there are over 60 cannabinoids in the cannabis plant (and thousands of other organic compounds)

• lipid solubility is very high, resulting in depot binding in fat tissue (and lipid membranes) - even after a single dose, traces of the drug can be found in the body for weeks afterwards
Cannabis (cont.)

- low doses of THC cause release of DA in the nucleus accumbens
- THC acts at the CB-1 receptor in the CNS
  - a targeted genetic mutation that blocks production of this receptor in mice abolishes the reinforcing effect of THC
  - it also abolishes the reinforcing effects of morphine and heroin
  - and reduces the reinforcing effects of alcohol
Cannabis (concluded)

• delta-9-THC is metabolized in the liver - the primary metabolite is 11-hydroxy-delta-9-THC, which is also psychoactive (perhaps even moreso)

• “wet” is a form of marijuana that has been soaked in other substances, often PCP, to make it seem more potent (sometimes called “embalming fluid”)

• marijuana was finally made completely illegal in the U.S. by the Marijuana Tax Act of 1937 - there are a good many conspiracy theories about this, none of which are well supported by evidence
The End

(next: Sleep and Biological Rhythms, chap. 8)