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DRUGS
AND
SOCIETY

U.S. PUBLIC POLICY

A different criterion for dependence potential can be the onset of withdrawal symptoms when the drug is not available after prolonged use. This measure is the traditional negative-reinforcement paradigm of addiction. Alcohol, heroin, and short-acting barbiturates get top billing by this standard (Jaffe and Martin 1990).

Another way to assess dependence potential is to measure the strength of the drug as a positive reinforcer. Users often self-administer a substance in order to induce euphoria, confidence, sensuality, or novel sensory experiences. This form of dependence is motivated primarily by a desire to repeat a rewarding experience rather than to avoid withdrawal symptoms. Cocaine, opiates, and amphetamines are probably the most addicting drugs by this standard (Bozarth 1989).

Finally, another measure of dependency is the drug's toxic severity per unit of time. In other words, how detrimental is the drug to the physical and psychological welfare of the person who is dependent on the substance for, say, a month or a year? By this criterion, smoked cocaine would probably compete with intravenous heroin as the most dangerous. Alcohol would likely rank second among common psychoactive substances (Hall, Room, and Bondy 1999).

COMPARATIVE TOXICITY

A literature review of approximately three thousand articles was conducted over a period of eight years in order to compare the acute lethality of commonly abused psychoactive substances. Readers should consult Gable (2004a, b) to obtain details regarding both the methodology and results of the review. The estimated lethal quantity of a substance was calculated using published data from laboratory-animal studies and from medical-examiner reports. Both the lethal dose and the effective dose listed in table 7.1 assume that the individual is a 70-kg adult human in good health who has not developed a tolerance to the substance as a result of prior use. The quantities refer to the weight or volume of the active material, not to the weight or volume of other substances that may be used as an extender, filler, or vehicle for the primary active ingredient.

An obvious difficulty in estimating lethal doses of illicit substances in non-laboratory situations is the unknown composition and purity of the administered material. For example, postmortem examination of six fatalities caused by material represented as methylenedioxymethamphetamine (MDMA or "ecstasy") found toxic or fatal blood levels of MDMA in only two decedents;

Table 7.1. Safety Ratio and Dependence Potential of Psychoactive Drugs¹

| <i>Substance</i> | <i>Effective Dose</i> | <i>Lethal Dose</i> | <i>Safety Ratio</i> | <i>Dependence Potential</i> |
|---|-----------------------|-------------------------|---------------------|-----------------------------|
| <i>Narcotics</i> | | | | |
| Heroin (iv) ² | 8 mg | 50 mg | 6 | Very high |
| Morphine (or) | 20 mg | 300 mg | 15 | High |
| <i>Depressants (sedative hypnotics)</i> | | | | |
| <i>Barbiturates</i> | | | | |
| Pentobarbital (or) | 250 mg | 5 g | 20 | Moderate/high |
| <i>Benzodiazepines</i> | | | | |
| Rohypnol (or) | 1 mg | 30 mg | 30 | Moderate |
| <i>Alcohol</i> | | | | |
| Ethanol (or) | 30 mg ³ | 300 mg | 10 | Moderate |
| <i>Stimulants</i> | | | | |
| Caffeine (or) | 100 mg ⁴ | 10 g | 100 | Moderate/low |
| Cocaine (in) | 80 mg ⁵ | 1.2 g | 15 | Moderate/high |
| Ephedra (or) | 25 mg | 3.5 g ⁶ | 140 | Moderate |
| MDMA (or) | 125 mg | 2 g | 16 | Moderate/low |
| Nicotine (sm) | 1 mg ⁷ | 50 mg | 50 | High |
| <i>Anesthetics</i> | | | | |
| Ketamine (in) | 70 mg | 2.7 g (?) | 38 (?) | Low |
| Nitrous oxide (inh) | 3.5 liters | 525 liters ⁸ | 150 | Moderate/low |
| <i>Hallucinogens</i> | | | | |
| LSD (or) | 100 mcg | 100 mg | 1000 | Very low |
| Mescaline (or) | 350 mg | 8.4 g (?) | 24 (?) | Very low |
| Psilocybin (or) | 6 mg | 6 g (?) | 1000 (?) | Very low |
| <i>Cannabis</i> | | | | |
| Marijuana (sm) | 15 mg | > 15 g | >1000 | Moderate/low |

¹ Adapted in part from Gable (2004a,b). The information presented here should not be used as a dosage guide. Significant differences exist with respect to a person's physiological and psychological reactions. The dosage indicated is the estimated median quantity for a 70kg adult human who has not developed tolerance to the substance.

² Routes of administration: in = intranasal (insufflation/snorting), inh = inhaled, iv = intravenous, or = oral, sm = smoked.

³ Approximately two 12-ounce beers or malt liquor at 5.5 percent by volume, or equivalent ethanol in other alcohol drinks.

⁴ Approximately 1.5 cups of 148 ml (5 oz.) of fluid coffee per cup.

⁵ Assumes three "lines" containing between 20 and 30 mg cocaine each.

⁶ Lethal dose not clearly established; estimate based on nonhuman animal studies.

⁷ Approximately one cigarette.

⁸ Nitrous oxide—when used with sufficient oxygen—has not been demonstrated to be lethal.

toxic or fatal blood levels of the more toxic paramethoxyamphetamine (PMA) were identified in all six cases (Byard, Gilbert, James, and Lokan 1998).

As previously noted, estimates of the effective dose depend, in part, on the intention of the user. The effective doses listed in table 7.1 are those most commonly used in social recreational situations by relatively inexperienced users.

: The term "safety ratio" rather than "therapeutic index" is used in table 7.1 because the intended uses of the substances are nonmedical in nature. The numbers are presented solely for the purpose of comparing the relative safety of substances not as a precise quantification.

Even though absolute magnitudes of risk remain uncertain, this quantification can give policy makers a basis for systematically ranking risks and for establishing priorities for intervention programs.

The "Dependence Potential" column in table 7.1 is an attempt to combine the positive- and the negative-reinforcement definitions of dependence potential summarized earlier. Combining physical and psychological dependency appears to result in a significant loss of information only for cocaine powder administered intranasally. The psychological dependence described in research reports for intranasal cocaine ranged from "moderate" to "very high," while the physical dependence ranged from "moderate" to "low."

A graphic representation of dependence and toxicity is presented in figure 7.1. The most dangerous substance (i.e., intravenous heroin) appears in the lower right corner because it has the highest dependence potential and the lowest safety ratio. In contrast, psilocybin ("magic mushrooms"), LSD, and marijuana are clustered in the upper left-hand corner because they have lowest dependence potential and the least acute physiological toxicity. Orally ingested psilocybin, with a safety ratio over 1,000, is one hundred times "safer" than alcohol with a safety margin of 10. Again, these are only estimates, but there seems to be little doubt about the relative position of most (but not all) of the substances with respect to their acute lethality.

A significant limitation of the two-dimensional comparison in figure 7.1 is best illustrated by the location of LSD. Although it is "safe" with respect to potential lethality and addiction, its potency in altering consciousness makes it much less socially benign than, say, caffeine. Driving a car after ingesting LSD is obviously less acceptable than after drinking a cup of coffee. The consciousness-altering potency of a substance and the conditions under which it is used must be factored into any comprehensive assessment of safety.

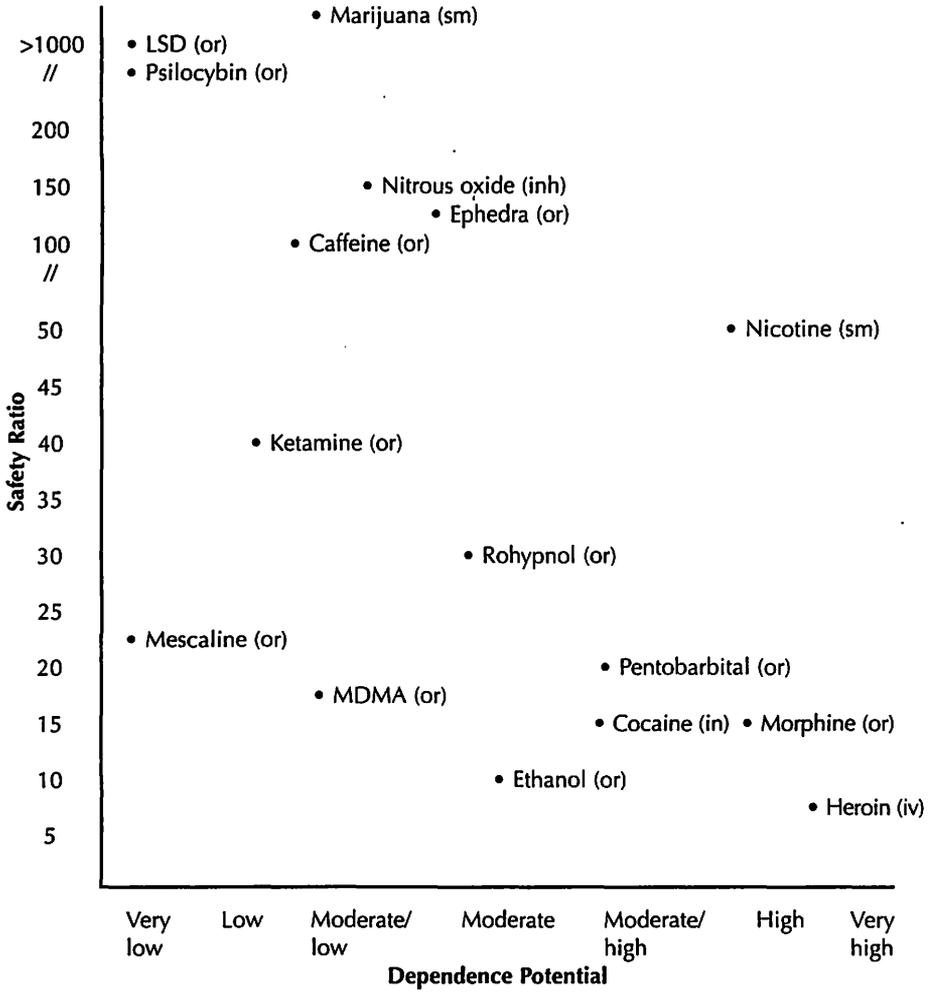


Figure 7.1. Safety Ratio and Dependence Potential of Psychoactive Drugs

DRUG REGULATION

Drug regulation in some form is generally agreed to be necessary. Unfortunately, many of our present drug laws are more symbolic than evidence based. Consider, for example, the Anti-Drug Abuse Amendments Act of 1988 (U.S. Code 21, § 1504), which stated, "It is the declared policy of the U.S. Government to create a Drug-Free America by 1995." The target date has come and gone, but the increased penalties that Congress imposed in 1988 for