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AN APPROACH TO DRUG CLASSIFICATION IN PSYCHOPHARMACOLOGY

Bruce H. Woolley,* Pharm.D.
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In our fast-paced society, numerous emotional and physiological factors often produce stress, anxiety, depression, and other dysfunctional behavior. One of the significant stressors that appear regularly where there are family and/or emotional problems is the use and abuse of drugs and substances which affect the central nervous system (brain and spinal cord). These agents can include prescribed drugs improperly taken, over-the-counter drugs purchased at local pharmacies or grocery stores, or illicit substances ingested for the “high” they seem to provide. However, when utilized and administered by competent medical personnel, these agents offer excellent palliation for psychopathology.

The therapeutic use of pharmacologically active drugs for behavioral dysfunctions requires competent diagnostic skills, expertise in clinical pharmacology, and proper monitoring techniques. Each involves years of preparation and training and are far beyond the scope of this paper. Within this context the author seeks to provide the reader with a survey of the major classifications of frequently prescribed and/or abused drugs only as a reference.

There have been many attempts in the literature to categorize and segment psychoactive agents. These attempts have varied, depending upon the reason for classification, from pharmacological approaches to pathological approaches to therapeutic approaches. All have merit and clearly show that any attempt at drug classification is, at best, superficial. Add to these attempts the ever-increasing abuse problem with psychoactive agents, and the problem of categorizing these agents becomes even more formidable.

For this paper the agents are classified into three categories (Table 1) utilizing a pharmacological approach and taking the chemical structure into consideration. Major drugs of abuse have been included to show action correlation. It must be kept in mind, however, that agents placed in one category can and do therapeutically and pathologically fall into other categories.

TABLE 1
Outline of Drug Classification

I. CNS DEPRESSANTS
A. NARCOTIC ANALGESICS
   1. Natural and semisynthetic opiate alkaloids
      a. Morphine
      b. Hydromorphone (Dilaudid)

   2. Phenylheptylamines
      a. Methadone (Dolophine)
      b. Propoxyphene (Darvon)

   3. Phenylpiperidines
      a. Meperidine (Demerol)
      b. Alphaprodine (Nisentil)
      c. Anileridine (Lentine)
      d. Piminodine (Alvodine)
      e. Diphenoxylate (in Lomotil)

   4. Morphinans
      a. Levomethadyl (Levo-Dromoran)
      b. Methorphan
      c. Levallorphan (Lorfan)

   5. Benzomorphans
      a. Phenazocine (Prinadol)
      b. Pentazocine (Talwin)

B. HYPNOTIC-SEDATIVES
   1. Barbiturates
      a. Ultra short acting
         Thiopental (Pentothal Sodium)
      b. Short acting
         Pentobarbital (Nembutal)
         Secobarbital (Seconal)
      c. Intermediate acting
         Amobarbital (Amytal)
      d. Long acting
         Phenobarbital
         Mepobarbital (Mebaral)
         Metharbital (Gemonil)

   2. Non-barbiturates
      a. Tertiary carbinols
         Ethchlorvynol (Placidyl)
         Ethniamate (Valmid)
      b. Piperidinediones
         Glutethimide (Doriden)
         Methyprylon (Noludar)
      c. Chloral derivatives
         Chloral hydrate (Noctec)
         Chloral betane (Beta-Chlor)
         Triclos (Triclos)
      d. Quinazolones
         Methaqualone (Quaalude)
      e. Monoureides
         Paraldehyde (Paral)
         Acetylcarbromal (Paxarel, Sedamyl)

C. TRANQUILIZERS
   1. Neuroleptics (antipsychotics or major tranquilizers)
      a. Phenothiazines
         1) Aliphatics (Aminoalkyls)

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Central Nervous System Depressants (Psycholeptics)

Generally, excluding the anesthetics, the CNS depressant substances can be divided into five divisions: the narcotic analgesics and antagonists, the sedative-hypnotics, the tranquilizers, the antiparkinson agents, and alcohol.

Narcotics

These drugs (Table 2) depress the centers in the brain and spinal cord and are used medically as analgesics (agents to relieve pain) as well as for their antitussive (cough relief) properties. They have a high potential for producing physiological and psychological dependence. Tolerance develops quite rapidly with these agents, and cross-tolerance exists in this category. The narcotics are divided into the natural and semisynthetic opiate alkaloids.

The opium alkaloids are contained in a white milky substance obtained from the unripe bulb of the poppy (Papaver somniferum). The milky substance expelled contains many drugs, including morphine, codeine, ethylmorphine, apomorphine, and papaverine. Morphine is the most important alkaloid; however, codeine is the most widely used.

1. Tolerance is a resistance and/or accommodation that is developed to the effects of the drug as that drug is chronically ingested. As a result of tolerance, over a prolonged period of time, more of the drug is needed to get the same effect one experienced with the initial dose.

2. Cross-tolerance refers to a condition in which tolerance to one kind of drug builds up and is carried over to other drugs. Drugs in many categories exhibit this property within their particular drug family.
Many other agents have been developed to produce analgesic and antitussive properties similar to the opiate alkaloids without the problem of dependency. However, dependency has proven to be a problem with all of these agents.

Usual short-term effects include sedation, analgesia, euphoria, and impaired intellectual functioning and coordination. Chronic effects include constipation, loss of weight and appetite, and temporary impotency or sterility together with dependence and tolerance.

**Sedative-Hypnotics**

One group of sedatives and hypnotics are derivatives of barbituric acid and are referred to as barbiturates. They induce a high degree of both physiological and psychological dependence and tolerance develops quite rapidly. Barbiturates (Table 3) are divided into four groups by their duration of action. The ultra short-acting barbiturates, such as thiopental (Pentothal), act very rapidly and have a duration of roughly an hour, depending upon the individual. The short-acting barbiturates, such as pentobarbital (Nembutal) and secobarbital (Seconal), react at a slower rate and have a duration of around three to four hours. The intermediate-acting barbiturates such as amobarbital and butobarbital have a duration of action between four and six hours. The classic example of long-acting barbiturates is phenobarbital, which has a duration of roughly an hour, five to eight hours.

**TABLE 3**

<table>
<thead>
<tr>
<th>Proprietary Name</th>
<th>Generic Name</th>
<th>Usual Single Adult Dosage</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>Morphine Sulfate</td>
<td>15mg</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Codeine</td>
<td>Codeine Phosphate</td>
<td>30-65mg</td>
<td>6 hrs</td>
</tr>
<tr>
<td>Heroin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilaudid®</td>
<td>Hydromorphone</td>
<td>2mg</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Percodan®</td>
<td>Oxycodone HCl</td>
<td>1 tablet</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Demerol®</td>
<td>Meperidine</td>
<td>50-100 mg</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Dolophine®</td>
<td>Meadonate</td>
<td>5-10 mg</td>
<td>4 hrs</td>
</tr>
</tbody>
</table>

Another group of sedatives and hypnotics (Table 4) is similar in action to the barbiturates, but is not a derivative of barbituric acid. In the past there was some question about whether these drugs produce real physiological dependence; however, as new data becomes available, evidence now points to a development of dependence. They are classified by their chemical structure and include the tertiary carbinols (Placidyl, Valmid), the piperidinediones (Doriden, Noludar), chloral derivatives (chloral hydrate), the quinazolones (Quaalude), and the monoureides (Paral, Paxarel). They are used in medical practice to induce sleep.

**TABLE 4**

<table>
<thead>
<tr>
<th>Proprietary Name</th>
<th>Generic Name</th>
<th>Usual Single Adult Dose</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doriden®</td>
<td>Guethemide</td>
<td>500 mg tablelets and capsules</td>
<td>5 hrs</td>
</tr>
<tr>
<td>Placidyl®</td>
<td>Ethchlorvynol</td>
<td>500 mg tablelets</td>
<td></td>
</tr>
<tr>
<td>Quaalude®</td>
<td>Mezicaqualone</td>
<td>150-300 mg capsules</td>
<td></td>
</tr>
<tr>
<td>Nocere®</td>
<td>Chloral hydrate</td>
<td>300 mg capsules</td>
<td>5 hrs</td>
</tr>
<tr>
<td>Noludar®</td>
<td>Methpylicon</td>
<td>300 mg capsules</td>
<td></td>
</tr>
</tbody>
</table>

**Tranquilizers**

Another subcategory of central nervous system depressants is tranquilizers. The tranquilizers are divided into two basic groups, the neuroleptics and anxiolytics, and are used medically in the treatment of psychoses and neuroses.

The neuroleptics (major tranquilizers or antipsychotics) include (1) the phenothiazines—including the aliphatics, the piperazines, and the piperidines; (2) the thioxanthenes, such as chlorprothixene (Taractan) and thiothixene (Navene); (3) the butyrophenones, such as haloperidol (Haldol), whose action resembles that of the piperazine phenothiazines; (4) the indoles, such as molindone (Moban); and (5) the dibenzoxazines such as loxapine (Loxitane) and chlorzapine. The neuroleptics are used to treat the psychoses.

The major drug-induced adverse reactions from neuroleptics are called extrapyramidal symptoms and are generally broken down into five distinct disorders or syndromes:

1. Tardive dyskinesia (Table 5) is a hyperkinetic
disorder developed by some patients on long-term antipsychotic therapy (particularly phenothiazines) which appears and persists after drug withdrawal. This disorder, at least at present, seems to be irreversible.

**TABLE 5**

Tardive Dyskinesia

1. Incidence may be as high as 15-20%.
2. Occurs more often in elderly patients, especially those with a history of brain damage.
3. May not become apparent until the antipsychotic drug is stopped or the dose reduced.
4. Characterized by stereotyped movements of the lips and tongue and sometimes of the trunk or extremities.
5. Antiparkinson drugs make it more severe. Symptoms are lessened by antipsychotic medication.
6. Duration of disorder may be from weeks to years.
7. Possibly due to elevated central levels of dopamine

2. Akinesia (Table 6) is a drug-induced disorder characterized by muscle rigidity and weakness.

**TABLE 6**

Akinesia

1. Occurs in about 15% of patients treated with antipsychotic drugs. In 90% of the cases it occurs within the first 72 hours of treatment.
2. Occurs more frequently in females over age 50 and more often with the aliphatic type of phenothiazines and butyrophenones.
3. Characterized by a mask-like face, reduced arm movement, shuffling gait, and rolling hand movements.
4. Readily controlled with traditional antiparkinson drugs.

3. Akathisia (Table 7) is the name for a condition of inner disquiet accompanied by an uncontrollable motor restlessness. The most frequently observed symptom is the patient's inability to sit or lie quietly.

**TABLE 7**

Akathisia

1. Incidence of about 21%. Seen generally after a few weeks of therapy.
2. Incidence is higher in young females.
3. Characterized by an inability to sit or stand still. Onset is often preceded by muscular discomfort.
4. Responds readily to treatment with traditional antiparkinson drugs.
5. Seen more frequently with piperazine phenothiazines.

4. Dystonic reactions (Table 8). The dystonias are acute disorders of muscle coordination, particularly in the face--e.g., grimaces, protrusion of the tongue, dysarthrias (imperfect articulation of speech), and oculogyric crisis. Other symptoms include tics, opisthotonos, and torticollis.

5. Dystonia is an acute disorder characterized by the impairment of the power of voluntary movement. This impairment results in fragmentary or incomplete movements.

1. Oculogyric crisis is an adverse reaction to antipsychotic medication which is characterized by a sudden turning up of the eyeballs. The patient is unable to move them and experiences severe pain due to the muscle spasms of the eye.
2. Opisthotonos--when a person's back muscles go into spasms causing his head and feet to bend backward and his torso to arch forward.
3. Commonly called wry neck, torticollis is a unilateral spasm of neck muscles. The most easily recognized symptom is the turning of the head to one side.

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**TABLE 8**

Acute Dystonic Reactions

1. Seen in only about 2% of treated patients.
2. Usually seen within 24-48 hours after drug administration has been instituted. Ninety percent of the cases occur within 4-12 days.
3. Seen more often in males under the age of 40 and in children.
4. Seen more frequently with piperazine phenothiazines and with haloperidol.
5. Characterized by oculogyric crisis, torticollis, and protrusion of the tongue.
6. Responds well to treatment with 50 mg of Benadryl.

The anxiolytics (minor tranquilizers) (Table 9) can lead to a psychological and physiological dependence, and tolerance is developed. They are divided into three groups: (1) the propanediol carbamates, (2) the diphenylmethane derivatives, and (3) the benzodiazepines. Most common short-term effects include drowsiness and fatigue. Effects of chronic ingestion include insomnia, delusions, and anxiety.

**TABLE 9**

Selected Anxiolytic Agents

<table>
<thead>
<tr>
<th>Proprietary Name</th>
<th>Generic Name</th>
<th>Usual Single Adult Dose</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propabenzyl</td>
<td>Benzyl</td>
<td>400 mg tablets</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Miltown</td>
<td>Methyl</td>
<td>400 mg tablets</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Diphenylmethane Antihistamines</td>
<td>Hydroxyzine</td>
<td>100 mg tablets</td>
<td>4 hrs</td>
</tr>
<tr>
<td>Antacids, Vistaril</td>
<td>Diphenhydramine</td>
<td>5-10 mg capsules</td>
<td>5 hrs</td>
</tr>
<tr>
<td>Benzoxyphene</td>
<td>Chlorpheniramine</td>
<td>25 mg capsules</td>
<td>5-5 hrs</td>
</tr>
<tr>
<td>Librium</td>
<td>Diazepam</td>
<td>2-5 mg, 5 mg, 10 mg tablets</td>
<td>5-5 hrs</td>
</tr>
<tr>
<td>Serax</td>
<td>Oxo8epam</td>
<td>10 mg, 15 mg, 30 mg capsules</td>
<td>5 hrs</td>
</tr>
<tr>
<td>Tranxene</td>
<td>Clozapine</td>
<td>7.5 mg, 15 mg, 20 mg capsules</td>
<td>5-5 hrs</td>
</tr>
</tbody>
</table>

**Alcohol**

Another category of depressants commonly used is alcohol. Usual short-term effects include central nervous system depression and impaired judgment, coordination, and reaction time. Chronic ingestion effects include possible obesity and irreversible damage to the brain and liver.

**Central Nervous System Stimulants (Thymoleptics)**

The central nervous system stimulants can be divided into three main divisions: the xanthine alkaloids (purines), the ecgonine derivatives, and the phenylethylamine sympathomimetic amines.

The xanthine alkaloids (purines) include theophylline, theobromine, and caffeine. Usual short-term effects include central nervous system stimulation, reduction of fatigue, and diuresis. Chronic ingestion and abuse dosages elicit such effects as insomnia, tolerance, and psychological dependence.

Ecgonine derivatives include cocaine and other miscellaneous atropine-like compounds. They are included here because of their high abuse and psychotoxic potential. Cocaine is obtained from the leaves of Erythroxylon coca trees and other species of
Erythroxylon. These trees are indigenous to Peru and Bolivia and have been used by the natives for centuries to increase endurance. There are many plants growing freely in almost all climates that are related to this alkaloid.

The third category includes the phenylethylamine sympathomimetic amines (Table 10). The major group of agents in this category is the amphetamines, but must also include other phenylethylamines with action similar to that of the amphetamines.

These agents have a potential for inducing both psychological and physiological dependence and they develop tolerance. Current medical uses include the treatment of narcolepsy and as a therapeutic agent for hyperkinetic children.

### TABLE 10

**Phenylethylamines (Sympathomimetic Amines)**

<table>
<thead>
<tr>
<th>Proprietary Name</th>
<th>Generic Name</th>
<th>Usual Single Adult Dose</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzedrine®</td>
<td>Amphetamine</td>
<td>2.5-5.0 mg</td>
<td>4-0 hrs</td>
</tr>
<tr>
<td></td>
<td>Sulfate</td>
<td>15 mg</td>
<td></td>
</tr>
<tr>
<td>Dexedrine®</td>
<td>Dextroamphetamine</td>
<td>2.5-5.0 mg</td>
<td>4-0 hrs</td>
</tr>
<tr>
<td></td>
<td>Sulfate</td>
<td>15 mg</td>
<td></td>
</tr>
<tr>
<td>Dexamyl®</td>
<td>Dextroamphetamine</td>
<td>2.5-5.0 mg</td>
<td>4-0 hrs</td>
</tr>
<tr>
<td></td>
<td>Sulfate</td>
<td>15 mg</td>
<td></td>
</tr>
<tr>
<td>Didrex®</td>
<td>Benphetamine</td>
<td>50 mg</td>
<td>4-0 hrs</td>
</tr>
<tr>
<td>Diphenhydramine*</td>
<td>Resin complexes of 2.5-5.0 mg</td>
<td>4-0 hrs</td>
<td></td>
</tr>
<tr>
<td>Methedrine®</td>
<td>Methamphetamine</td>
<td>2.5-5.0 mg</td>
<td>4-0 hrs</td>
</tr>
<tr>
<td>Desoxyn®</td>
<td>Hydrochloride</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Psychotomimetics (Hallucinogens or Psychodysleptics)**

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Chemical Name</th>
<th>Usual Single Adult Dose</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSD</td>
<td>Lysergic acid diethylamide tartrate</td>
<td>150-400 mg</td>
<td>12 hrs</td>
</tr>
<tr>
<td>Psilocin</td>
<td>Dimethylated hydrazine</td>
<td>75 mg</td>
<td>6 hrs</td>
</tr>
<tr>
<td>DET</td>
<td>Dextramylamine</td>
<td>0.7 mg/kg</td>
<td>1/2-2 hrs</td>
</tr>
<tr>
<td>DMT</td>
<td>Dimethyltryptamine</td>
<td>0.7 mg/kg</td>
<td>1/2-2 hrs</td>
</tr>
<tr>
<td>MDA</td>
<td>Methylene dimethoxy-phenethylamine</td>
<td>100 mg</td>
<td>12 hrs</td>
</tr>
<tr>
<td>STP</td>
<td>4-methyl-2.5-dime-thoxy-methylene-phenethylamine</td>
<td>3.2-10.0 mg</td>
<td>4-24 hrs</td>
</tr>
<tr>
<td>Peyote</td>
<td>Tryptamines or ypsilocin</td>
<td>1/2-3/4 oz or</td>
<td>14 hrs</td>
</tr>
<tr>
<td>(Mescaline)</td>
<td>(Methylated catecholamines)</td>
<td>4-12 buttons</td>
<td></td>
</tr>
</tbody>
</table>

**Mood Modifiers**

### Antidepressants

*Monoamine oxidase (MAO) inhibitors.* MAO inhibitors can be divided into the hydrazines and the nonhydrazines. They are used as antidepressants, and the dosage varies with each individual agent. Isocarboxazid (Morplan) and tranylcypromine (Parnate) are the most potent on a milligram per milligram basis, and nialamide (Niamid) is the least potent. MAO inhibitors have numerous adverse effects including insomnia, hallucinations, muscle weakness, headache, dryness of the mouth, and blurred vision. Other effects include hypotensive reactions, infrequent anorexia (loss of appetite), hepatobiliary reactions, and inability to ejaculate.

**Tricyclic antidepressants.** Tricyclic antidepressants are divided into the dibenzazepine derivatives (Tofranil and Fertoane or Norpramin) and the dibenzocycloheptadiene derivatives (e.g., Elavil and Aventyl). Another compound, doxepin, (Sinequan) is closely related to the dibenzocycloheptadiene derivatives.

**Psychotomimetics (Hallucinogens or Psychodysleptics)**

The psychotomimetics (Table 11) are agents with no currently accepted medical use. They produce minimal to moderate psychological dependence, and tolerance can develop. It should be pointed out that even though these drugs are classified as "hallucinogens," they do not cause true hallucinations every time they are used. Many times they cause the person who abuses these substances to perceive the environment in a distorted form—synesthesia, not strictly hallucination. The psychotomimetics can be classified into four agents or groups of agents. These are mescaline, psilocin, lysergic acid derivatives, and the tryptamines.

**Mescalin is a pharmacologically active alkaloid from various species of the cactus Lophophora.** The top of the aerial shoots is cut off and dried, the needles removed, and what is left is called a peyote button or mescal button. Mescaline is a phenylethylamine and has actions similar to those agents.

Psilocin comes from the sacred Mexican mushroom (Psilocybe mexicana). It is an alkaloid with phenylethylamine properties and is reported to be up to 100 times more potent than mescaline.

Lysergic acid derivatives are numerous. Many plants including morning glory seeds and ergot, are precursors to lysergic acid. Ergot comes from the rye plant in the form of a copper-colored rust that grows around the top when the plant remains too moist. The most commonly abused lysergic acid analog is LSD (d-lysergic acid diethylamide tartrate). The dose of LSD is 1/40,000 gm.

Tryptamines are generally shorter acting than the lysergic acid derivatives. Lysergic acid "trips" can range up to a day in length. Tryptamines last two hours. Dimethyltryptamine (DMT) is sometimes called "businessman's trip" and lasts about 45 minutes. Diethyltryptamine (DET) lasts about two hours and is similar to DMT.

Usual short-term effects of the psychotomimetics include visual imagery, increased sensory awareness, anxiety, nausea, and impaired coordination and sensory perception. Chronic ingestion effects are generally no different from short-term effects; however, long-term use has been shown to produce a more pronounced panic reaction.
CANNABIS (Marihuana)

Cannabis is not a narcotic, not a depressant, not a stimulant, not a tranquilizer, and not a hallucinogen—although it has properties similar to each of these. In animals, cannabis potentiates barbiturate sleep time. It also potentiates amphetamine stimulation in animals. All the Agents listed under psychotomimetics have cross tolerance; however, cannabis does not have cross tolerance with the hallucinogens.

Use of cannabis creates a moderate psychological dependence, and it has moderate tolerance potential. Cannabis is not a single substance. A number of different varieties have been isolated. Examples of various types include Cannabis sativa, Cannabis indica, Cannabis americanus, and Cannabis mexicana. Differentiation has been made between several varieties such as michoacan, columbian, and synsimillia. These varieties can have such a low potency that the person ingesting the substance has almost no discernible effect. On the other hand, there are some varieties that have shown toxic manifestations in the nerve pathways in the brain.

Usual short-term effects include relaxation, euphoria, increased appetite, and possible impairment in judgment, time perception, and coordination. Possible long-term effects include subtle personality changes and diminution of intellectual acuity.

Conclusion

The drugs or agents mentioned, as well as the terminology presented, are given as an overview with the expectation that there will be a closer health professional team relationship. This closer relationship can lead to more adequate understanding of and rapport with patients who are being treated (or are otherwise involved) with agents having an effect on mood, perception, and behavior. This presentation is made with the hope that better management and monitoring of the patient will occur to reduce possible drug side effects and adverse reactions or interactions.

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