Psychedelics / Hallucinogens

Psychology 472
Pharmacology of Psychoactive Drugs

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Psychedelic Drugs

• Many Types
• Broken out by the type of NT it affects
  – Anticholinergic
  – Catecholamine-like
  – Serotonin-like
  – Psychedelic Anesthetics

Pharmacokinetics

• Most taken orally
• Some smoked (e.g., PCP, DMT)
• Taken by circulatory system to receptor sites
• Metabolized by the liver
  – Some material can remain for a long time
  – Most drugs are metabolized in 6-8 hours

Pharmacodynamics

• Site of action depends on the drug

Anticholinergic

• Scopolamine
• Is an acetylcholine (ACH) antagonist
• Blocks ACH from binding on its receptors
• Is widely distributed in plants
  – Atropa Belladonna (deadly nightshade)
  – Datura Stramonium (Jamestown weed, stinkweed, Jimsonweed, Thorn Apple)
  – Mandragona Officinarum (Mandrake)
• Acts on both the PNS and CNS

PNS

• Causes
  – Dry mouth
  – Dry skin
  – Increased body temperature
  – Blurred vision
  – Tachycardia
  – Hypertension
  – others
CNS Effects

• Depends on the dose

Low Dosages

• Drowsiness
• Mild Euphoria
• Amnesia
• Fatigue
• Delirium
• Dreamless Sleep
• Others
• Generally clouds consciousness and produces amnesia

Moderate Doses

• Get more restlessness
• Excitement
• Hallucinations
• Euphoria
• Disorientation
• Others

High Doses

• Develops into a Psychotic State
  – Delirium
  – Mental Confusion
  – Stupor
  – Coma
  – Respiratory Depression

Issues

• Can create excitement and loss of control
• Clouds consciousness (Cannot recall what you did)
• Decreases memory
• Results
  – Is not as attractive as other hallucinogens
  – Low use rates

Catecholamine-Like

• Mescaline
• DOM (STP), MDA, DMA, MDMA, TMA MDE
• Myristin, Elemicin

• Resemble NE and Dopamine
• Are mixed serotonin and dopamine receptor agonists
• Generally, bind on the 5-HT$_{2a}$ receptor
Mescaline
• Comes from the Peyote plant
• Is a spineless cactus with a small crown or “button” on its top.
• Button is cut and dried
  – (called mescal button)
• Is softened in the mouth and swallowed

Use
• Is primarily used in Native American religious ceremonies.
• Is legally available for religious use
• Used to gain insight by the user

Effects
• Is absorbed rapidly and completely
• Get adequate brain concentrations in 1-2h
• 3.5 - 4 hours causes effects (usually visual)
• Lasts for approx. 10 hours
• Is not metabolized before being excreted.
  – One of a few drugs to do so

Brain Effects
• Works on frontal lobe (especially right hemisphere)
• Produces unusual psychic effects and hallucinations

Behavioral Effects
• Anxiety
• Tremors
• Visual hallucinations (Bright lights, geometric designs,
  Color and space perception is impaired
• Can often recall information

DOM (STP), MDE, DMA, TMA
MDA, MDMA,
• Are similar to mescaline and methamphetamine
• Produce similar effects
• Psychedelic effects increase as doses increase
• Are more potent than mescaline
Dimethoxy-Methamphetamine (DOM)

- Also called STP
- Effects are similar to mescaline but 100 times more potent
- Is less potent than LSD
- Highly associated with overdoses
  - Convulsions, Death
- Got a bad reputation
- Not often used anymore

Designer Psychedelics

- Are structural variations of amphetamine
- Many types
  - Methylene-dioxy-amphetamine (MDA)
  - Dimethoxy-methyl-amphetamine (DMA)
  - Methylene-dioxy-ethylamphetamine (MDE) also called Eve
  - Trimethoxy amphetamine (TMA)

Effects

- Resemble mescaline and LSD
- Are a mix of catecholamine and serotonin interactions
- Side effects are similar to MDMA

MDA

- Is a metabolite of MDMA (Ecstasy)
- May be the active ingredient of MDMA
- Causes serotonin and dopamine release
  - Actually stimulates serotonin receptors more than MDMA
  - Causes more psychedelic-like effects
  - Has more stimulant / psychedelic hallucinogenic qualities
  - Less intense empathogenic properties
- Is less predictable than MDMA

MDMA / Ecstasy

- Variety of street names
  - XTC
  - Adam
  - M
  - M
  - Essence
  - E
  - Others

Effects

- Resembles MDA in structure
- Is less hallucinogenic than MDA
- Fewer visual distortions
- Lots of side effects
Effects on Neurons

• Causes an increase of serotonin in the synaptic cleft
• Then blocks the reuptake of serotonin from the synaptic cleft
• Does the same thing with Dopamine neurons

Reported Positive Effects

• Enhanced mood
• Increased emotional sensitiveness
• Little anxiety
• No hallucinations
• Heightened sensory awareness
• Increased psychomotor drive
Side Effects

Adverse Neuronal and Brain Effects

- Down Regulation
- Reduces the number of post synaptic receptors

Major Long Term Effects

- Is a potent and selective neurotoxin to serotonin neurons
- Serotonin levels and metabolites are reduced
- Damages presynaptic elements
  - Terminals degenerate
- Damage remains at least two years and probably forever
Conclusions about MDMA

- Is seen as safe by users
- Is really bad stuff even at low doses
- Look at reviews in NIDA

Other Stuff

- Have Herbal Ecstasy
  - Combines ephedrine and caffeine
  - Very dangerous for overdose
  - Hypertension
  - Cardiac Arrhythmias
- Candyflipping
  - Combines MDMA and LSD
  - Produces a synergistic effect

Myristin, Elemicin
Myristin, Elemicin

- Myristin (Nutmeg)
- Elemicin (Mace)
- Are common spices
- Usually put in tea 1-2 tsp
- Effects occur in approximately 2-5 hours

Effects

- Feelings of unreality
- Euphoria
- Visual Hallucinations
- Disorientation
- Confusion

Side Effects

- Feelings of impending doom
- Acute psychotic reactions
- Nutmeg
  - Also produces nausea, vomiting, tremors
  - Usually prevents repeat usage

Serotonin-Like

- Also called Indoleamines
- Lysergic Acid Diethylamide (LSD)
- Dimethyltryptamine (DMT)
- Psilocybin, Psilocin, bufotenine
- Ololiuqui (Morning Glory Seeds)
- Harmine

Effects

- Work on Serotonin receptors
- Produce psychedelic effects
- Causes distortion of sensory inputs

LSD

- First synthesized by Albert Hoffman in 1938
- Major research using LSD began in the 1950’s as part of research investigating psychotic behavior
- Has been used as part of psychotherapy in very low doses (not street levels)
**Effects**

- Is distributed through the body
- Enters the brain in about 60 minutes
- Effects last about 6-8 hours (depends on the dose)
- Is very potent

**Alterations in Perception**

- Get changes in thinking, mood, emotion
- Time is slowed
- Sensory input intensifies
- Visualize imagined objects
- Visual alterations
- Colors may be heard
- Sounds may be seen
- Others

**Phases**

- Somatic Phase
  - Where absorption occurs and body changes occur
- Sensory/Perceptual Phase
  - Where sensory distortions and pseudo hallucinations occur
  - Desired phase
- Psychic Phase
  - Changes in mood,
  - Disruption of thought process
  - True hallucinations occur
  - Not desired - Bad Trip

**Tolerance**

- Get tolerance to the drug
- Get cross tolerance to other psychedelics
- Lost after several days of not taking the drug
- No physical dependence
- Few withdrawal effects occur (if any)

**Side Effects**

- Increased
  - Heart rate
  - Blood Pressure
  - Pupils Dilate
  - Drowsiness
  - Sometimes nausea
- Overall, Is a relatively safe drug

**Dimethyl-Tryptamine (DMT)**

- Is an active ingredient in some plants
- Produces effects similar to LSD
- Binds to serotonin receptors
- Is usually snorted or smoked (not Oral)
- Onset 2 minutes
- Effects last 30 minutes
- Called businessman’s lunch or LSD
Effects

- Increased HR, BP, Temperature, etc
- Increased endorphin levels
- Causes
  - visual hallucinations
  - Intoxication
  - Loss of awareness to surroundings

Psilocybin and Psilocin

- Are agents found in some mushrooms
- Resemble but are less powerful than LSD
- Peak effects in about 2 hours
- Lasts about 6-8 hours
- Are taken orally
- Are used in some Native American ceremonies

Ololiuqui

- Found in morning glory seeds
- Used for spiritual communication
- Are about 1/10th as powerful as LSD
- Are still potent

Conclusion

- Most are safe
- Cause a wide variety of sometimes powerful effects

Psychedelic Anesthetics

- Phencyclidine (Sernyl)
- Ketamine (Ketalar)
- Were developed for anesthesia
- Both produce a psychedelic state
- Psychedelic effects are unique - Do not involve Serotonin, ACH or Dopamine neurons

Phencyclidine (Sernyl)

- Angel Dust, Super grass, Killer Weed, Rocket Fuel
- Was developed as an anesthetic
- Abandoned because of reactions in surgery
- Still used as an immobilizing agent in veterinary anesthesia in large animals
- Blocks Ca influx via Glutamate NMDA receptors
### Effects
- Detachment,
- Slurred Speech loss of coordination
- Auditory hallucinations
- Severe mood disorders
- Amnesia
- Others

### Side Effects
- Acute anxiety
- Paranoia
- Feeling of impending doom
- Violent hostility
- Symptoms often resemble an acute psychotic disorder and may become permanent
- Resembles schizophrenia psychotic states
- Can be very dangerous

### Ketamine (Ketalar)
- **Other Names**: Special K, K
- **Is a general anesthetic for humans and animals**
- Produces effects similar to PCP
- Produces visual effects similar to LSD

### Effects
- Overt hallucinatory effects are short lasting (one hour)
- **Effects**
  - Judgment
  - Senses
  - Coordination
- Get from diverted supplies and vet. Clinics, etc.
- Are starting to see at rave parties

### Sites of Action for PCP and Ketamine
- Block N-Methyl-D-aspartate (NMDA)/glutamate receptors
- Glutamate is an excitatory NT
- Induces a schizophrenic effect
- NMDA blockers are among the best amnesic drugs known
- May be useful for head trauma

### NMDA Receptors
- Is a glutamate ionotropic receptor for calcium ions
- Are widely distributed in the brain and SC
- High concentrations in the hippocampus and cortex
- May aid in protecting brain tissue following trauma or strokes
Hallucinogens
In General
• For the most part, have high LD50 levels.
• Are some of the most potent drugs
• Create a wide variety of effects