Psych 181: *Dr. Anagnostaras*

Lecture 4

Behavioral Pharmacology

Behavioral Pharmacology

Behavioral Pharmacology

The study of the relationship between the physiological actions of drugs and their effects on behavior and psychological function

- Drugs do not create behaviors outside the normal species-typical repertoire
- They alter the probability of occurrence of behaviors

Set and setting

The behavioral effects of drugs are due to complex interactions amongst the pharmacological actions of drugs, the state of the organism ("set"), and the environmental circumstances surrounding drug administration ("setting")

Evaluating the behavioral effects of drugs

Primary Evaluation

Unconditioned effects on behavior

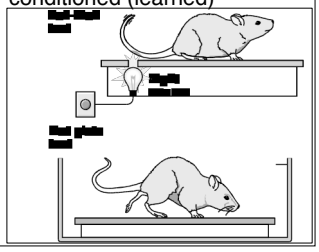
- Motor activity
  - locomotion, catalepsy, balance, strength
- Seizures
- Eating and drinking

Secondary evaluation

Tests of more specific functions

(either unconditioned or conditioned (learned)

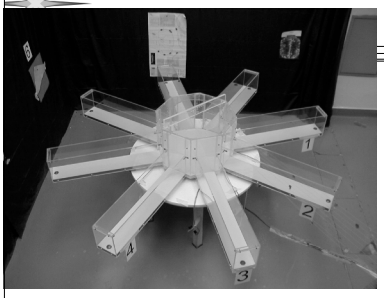
- Analgesia



Secondary evaluation

- Learning and memory
  -several different forms

Spatial Radial Maze Task



"Win-Shift"

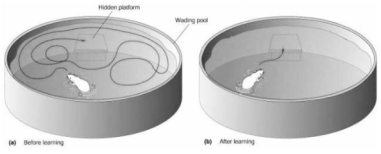
Lots of spatial (room) cues

Rats/mice use these cues to avoid revisiting arms (ecologically valid)

All arms baited, must not revisit arms

•Different brain systems than non-spatial

Morris water maze test of hippocampal function

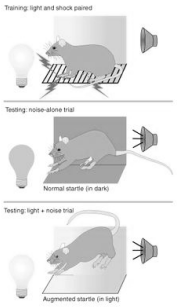


•Use spatial cues in room (posters, etc) to locate submerged platform (same place ea. time)

•Measure latency to mount plaform & swim path (distance traveled to platform)

•Different brain systems than visible platform

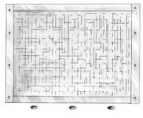
► **Method Used by Davis and His Colleagues to Investigate the Augmented Startle Response**



Source: Adapted from Davis, M., *Trends in Pharmacological Sciences*, 1992, *13*, 35–41.

► **Nonrecurring-Items Delayed Nonmatching - to - Sample Test**

1 The monkey moves the sample object to obtain food from the well beneath it.



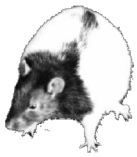
2 A screen is lowered in front of the monkey during the delay period.

3 The monkey is confronted with the sample object and an unfamiliar object.

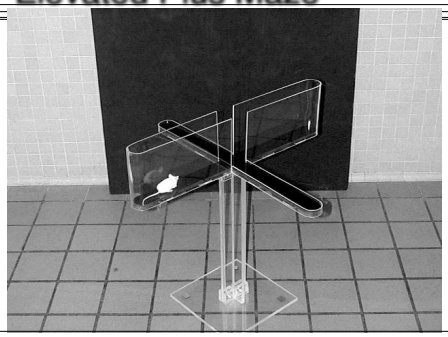
4 The monkey must remember the sample object and then select the unfamiliar object to obtain the food beneath it.

Source: Adapted from Mishkin & Appenzeller, *Scientific American*, 1987, *256*, 80–89.

Fear and Anxiety (Mon)



Secondary Eval •• Anxiety •• Elevated Plus Maze



Secondary evaluation

- Learning and memory
- Anxiety
- Schedule-controlled behavior

Schedules of reinforcement

Positive reinforcement

Presentation increases the probability of the preceding behavior

Negative reinforcement

Removal increases the probability of the preceding behavior

Punishment

Decreases the probability of a behavior

Ratio schedules

Reinforcement is based in the number of responses made

- Fixed vs. variable (FR vs. VR)
  Continuous reinforcement (FR1)

Interval schedules

Reinforcement is based on the amount of time that has elapsed since the last reinforcement

- Fixed vs. variable (FI vs. VI)

DRL schedules
(differential reinforcement of low rates)
Version of a FI; get reinforcement after fixed time, but if respond before time is up causes "time out" and resets clock

Schedules of reinforcement

Operant procedures used for two primary reasons:

1) To ask questions about the stimulus properties of drugs ("what does it feel like")
2) To ask questions about the reinforcing and/or incentive properties of drugs ("will you work for it")

Drugs as discriminative stimuli

S_D = stimulus that signals availability of reinforcement (e.g., red vs. green light)

Animals learn to respond when appropriate S_D is present

Drugs can serve as a S_D

- Animals learn to respond appropriately in presence of drug S_D
- S_D is related to interoceptive cues of drug

Drugs as discriminative stimuli

Method to ask animals about the interoceptive cues associated with different drugs

Press left lever if on morphine > get food
Right lever if given saline > get food

Give new drug - is it like morphine?

- Left lever - Yes
- Right lever - No

Drugs as discriminative stimuli

Using drug discrimination techniques find that animals classify drugs just like humans

E.g., amphetamine and cocaine alike, but different than morphine, but morphine like heroin and other opiates

Measurement of drug reward

Goal is to determine abuse potential of different drugs and to study mechanisms by which drugs produce rewarding effects and dependence

- Measure effects on withdrawal symptoms
- Self-administration paradigms
- Conditional place preference

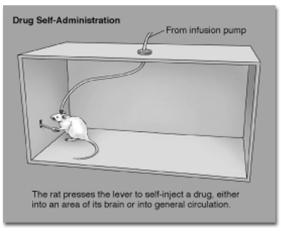
Effects on withdrawal

Steps:

- Produce physical dependence with prototypical drug (e.g., morphine)
- Withdraw and give unknown
- If block withdrawal symptoms will probably produce similar dependence syndrome
  (Not conclusive)

Self-administration paradigms

- Two Behavioral Paradigsms



Self-administration paradigms

Procedures:

- Substitution procedures
- Choice procedures

Predictive validity: All drugs self-administered by animals are also self-administered by people

Self-administration paradigms

Drugs that maintain self-administration

amphetamines, barbiturates, cathinone, cocaine, codeine, ethanol, fentanyl, heroin, methadone, methamphetamine, MDMA, methylphenidate, morphine, nicotine, PCP, THC

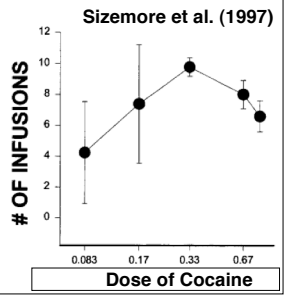
Drugs that do not

aspirin, haloperidol, imipramine, lidocaine, mescaline, LSD

Self-administration paradigms

FR Schedules

- typical measure rate or number of responses (or infusions)
- inverted U curve

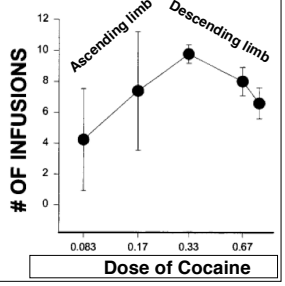


Self-administration paradigms

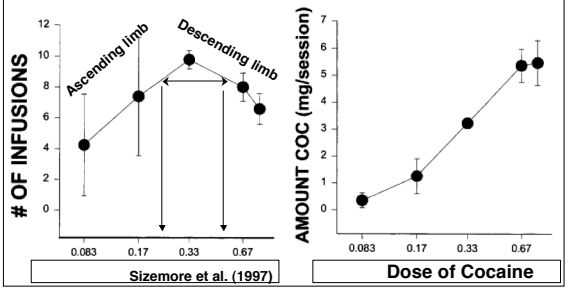
FR Schedules

Descending limb?

- incapacity
- satiety
- loss of reward



Self-administration paradigms



Self-administration paradigms

FR Schedules

On ascending limb typically assume:

- increase in rate = increase in reward

On descending limb, typically assume:

- decrease in rate = increase in reward

  {increase in rate = decrease in reward (represents a compensatory response to loss of reward)}

Self-administration paradigms

Increase in rate = decrease in reward

Fits dopamine (DA) antagonist studies

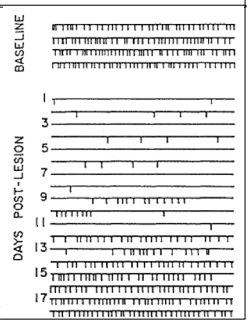
- DA antagonists increase rate (as does decreasing dose)

Homepage.mac.com/sanagnos/psyc181.html Self-administration paradigms

Problem

E.g., 6-OHDA lesion

(decreased rate interpreted as decreased reward)

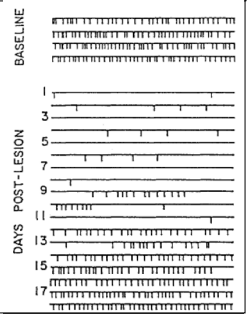


Roberts et al. (1980)

Self-administration paradigms

Problem

"How can both an increase and a decrease in rate of drug intake be used to draw the same conclusion? The dilemma is unmistakable: rate is an ambiguous measure of reinforcing efficacy" (Arnold & Roberts, 1997)

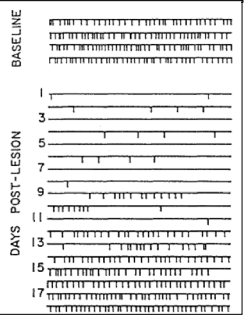


Self-administration paradigms

Problem of rate is old issue

Electrical self-stimulation

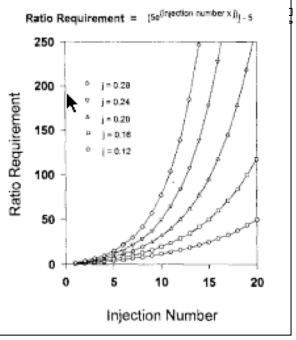
Faster rate with lower of two current intensities, but choose higher of two intensities
(Hodos & Valenstein, 1962)



Self-administration paradigms(X)

Progressive ratio schedules

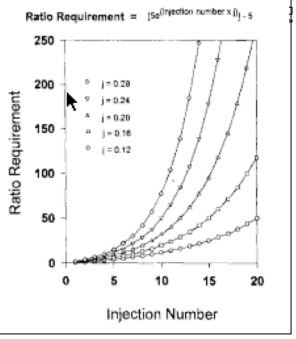
Progressive increase in responses required
1, 2, 4, 6, 9, 12, 15, 20, 25, 32, 40, 50, 62, 77, 95, 118, 145, 178, 219, 268, 328, 402, 492, 603 ...
(j = 0.20)



Self-administration paradigms

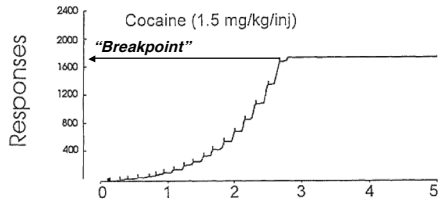
Progressive ratio schedules

Measure of motivation to take drug (how hard will will work for it), defined by "breakpoint"



Self-administration paradigms

"Breakpoint"
(highest ratio achieved)

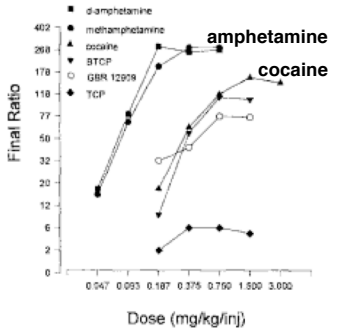


Self-administration paradigms

"Breakpoint"

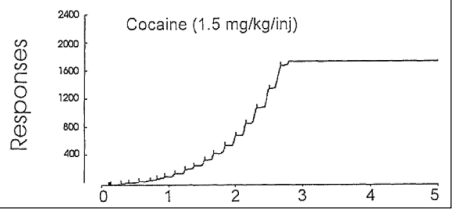
Comparing different drugs

DA antagonists vs. 6-OHDA



Self-administration paradigms

Problems: One data point, cumulative dosing, etc.



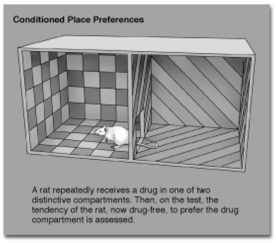
Conditioned place preference

Pavlovian context conditioning procedure

- Pair drug administration with place in environment
- Take advantage of a principle of reward
  - stimuli that are rewarding, “elicit approach responses and maintenance of contact with the stimulus”
- On test day: measure where spend time

Conditioned place preference

- Two Behavioral Paradigms (continued)



Conditioned place preference

Advantages

- Simple
- Limited training required
- Test in non-drug state

Disadvantages

- Not measure drug reward but rewarding properties of secondary reinforcer

Sample question

Which schedule of reinforcement is used to calculate "breakpoint"?

(a) FR10
(b) VI15
(c) DRL schedule
(d) Variable ratio
(e) Progressive ratio