Psychopharmacology: Understanding the Medications the Veterinarian Prescribes, Including Legal and Ethical Issues Regarding Their Use

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Why would we use psychoactive medications on animals?
All behavior occurs because of chemical reactions in various parts of the brain.

To properly understand what psychoactive medications to use and how to use them, you need to know:

- Neuroanatomy
- Neurophysiology
- Neuroendocrinology
- Neurochemistry
- Neuropharmacology
- Normal species specific behavior
- Etiology of behavior disorders
- How specific disorders respond to specific medications
Normal variation vs. Pathology
Causes???

- Genetics
- Physical trauma
- Psychological trauma
- Metabolic disease
- Infectious disease
- Teratology
When might medication be indicated?

- Cat’s behavioral disorder (anxiety, phobias, OCD) is so severe that normal environmental management, behavior modification and training techniques are insufficient to bring about improvement, either at all or at an acceptable rate of progress.

- What defines “acceptable”
  - What the owner considers acceptable. Owners vary widely in their tolerance of various problems
  - With advice from their veterinarian and their feline behaviorist regarding realistic expectations and ways to cope with the problem(s)
Veterinary Behavior

- Practice of veterinary medicine:

- To diagnose, treat, correct, change, relieve or prevent animal disease, deformity, defect, injury, or other physical or mental conditions; including the prescription or administration of any drug, medicine, biologic,...or to render advice or recommendation with regard to any of the above.

- Model Practice Act, AVMA
Professional Responsibilities

- When an animal has a clinical sign that is physical or behavioral in nature only a licensed veterinarian can legally
  - Diagnose
  - Prescribe a treatment program
  - Prescribe medication
- When non-veterinarians do either of the first two, they are practicing veterinary medicine without a license.
Clinical sign???

- Not within the range of normal and expected behavior for that species, given their sex and age
  - Mother cat who has not previously been aggressive gives birth. She is a good mother, but snarls at strangers approaching the nest to look at the kittens. If they reach their hand in, she will bat at them with claws extended.
    - Normal or not?
  - A cat that has historically been friendly starts running away from its owners if it sees them. If they catch it by surprise and manage to touch it or pick it up, it bites them.
    - Normal or not?
Veterinary Behavioral Medicine is not dog (or cat) training

- Teaching a behaviorally normal animal to
  - Sit
  - Down
  - Heel
  - Come
  - Jump
  - Etc.
- using appropriate training techniques is training
- Giving advice on environmental management to provide an animal with optimal welfare that minimizes the likelihood of the development of behavior problems is the practice of applied animal behavior

- Determining if an animal that has become aggressive to its owner has
  - Fear aggression
  - Rabies
  - Psychomotor epilepsy
  - A greenstick fracture of the humerus
  - Play aggression
  - Hyperthyroidism
  - Ear mites
  - Etc., Etc., Etc.
- is the practice of veterinary medicine
Stress

Medical Problem

Stress

Behavior Problem

Owner upset

Medical Problem worse

More stress

Helping the cat needs team approach
Owner↔Veterinarian↔Behaviorist↔Veterinary Technician↔Other
Psychoactive Medications

- Medications that produce changes in behavior and/or motivation
- Most use of psychoactive medications in veterinary medicine is extra-label.
- ONLY exceptions are
  - Anipryl® for Canine Cognitive Dysfunction
  - Clomicalm™ for Canine Separation Anxiety
  - Reconcile™ for Canine Separation Anxiety
Cats???

- There are no FDA approved medications for cats with behavioral disorders.
Animal Medicinal Drug Use Clarification Act (AMDUCA 1994)

This law defines the conditions under which veterinarians can prescribe medications in an “Extra-Label” status

- Valid client/veterinarian/patient relationship
- Medical and, in the case of psychoactive drugs, Behavioral history MUST be taken
- Veterinarian has physically examined the animal
- Veterinarian has established a diagnosis and the need for treatment
- Must be a specific rationale, and its use is accepted under current state of the art of behavioral medicine.
Extra-label usage

- Inform client of the extra-label status of the drug.
- If necessary, explain to the client what extra-label means.
- Inform the client of known side-effects.
- Signed informed consent statement.
While the veterinarian can obtain valuable information and assistance from:

- Veterinary Technicians who are educated and experienced in techniques of treating animal behavior
- PhD’s who focus on domestic and applied animal behavior
- Ethical trainers who use humane training techniques
- Other behaviorists

The veterinarian is legally and ethically responsible for all decisions regarding treatment of a given case.
What should behaviorists working with cats do when a the problem is severe enough that a veterinarian needs to be involved?

- Give the veterinarian factual information about what you have observed
- Advise the owner about factual information that they need to relay to the veterinarian
- Video/audio recordings of the cats behavior, are often useful
  - Problem behavior
  - Normal, acceptable behavior
What to do when a problem is so severe it is beyond the experience of area GPs?

- American College of Veterinary Behaviorists
- Recognized by the AVMA 22 years ago, in 1993
- [http://www.dacvb.org/about/member-directory/](http://www.dacvb.org/about/member-directory/)
ACVB

- Pre-vet post secondary education, usually 4 years
- Veterinary school-4 years
- One year general internship or equivalent
- Clinical residency, usually 3 years
- Pass comprehensive, 2-day exam
How can DACVBs help?

- Telephone, Skype or similar consulting with GP’s
- DACVB’s at universities often do this for no charge
- DACVB’s in private practice usually charge a fee
PSYCHOACTIVE MEDICATIONS

- Drugs labeled for human psychiatric problems may have different efficacy, side-effect profiles and toxicities in companion animals.
- Economics is very different. Most psychoactive medication use is paid for out of pocket by the owner.
Psychoactive medications are most effective when used as an adjunct to behavior modification and environmental management.

It is extremely rare for a pill to provide a “cure”.

Alleviation of anxiety and distress can make it possible to conduct behavior modification such as desensitization and counter-conditioning.
General Characteristics

1. Metabolized in the liver
2. Excreted in the urine or urine and feces
3. Since long term use is common when treating behavioral problems, ensure that kidneys and liver are functioning adequately
4. Tests for liver and kidney function are not because the drugs damage these organs, but because these organs must be functioning correctly for elimination to occur at a normal rate
5. Most psychoactive drugs pass through the placenta and enter the milk
Antipsychotics
Phenothiazine Neuroleptics

- Acepromazine maleate - Most widely used phenothiazine neuroleptic in veterinary medicine
In Animals

- Produces **general behavioral quieting**, but does not have a specific **anxiolytic effect**. Useful for temporarily decreasing motor activity.

- **Not indicated for long-term treatment of thunderphobia, separation anxiety or other fear-related disorders**

- Anecdotal evidence that chronic use may result in exacerbation of noise-related phobias
Side Effects

- **Sedation**
- **Ataxia** (unsteady, staggering)
- **Aggression** (even in animals that have never shown aggression)
- **Hypotension** (low blood pressure)
- **Bradycardia** (slow heart beat)
- **Hypothermia**
Side Effects

- Hypothermia
- Antiemetic-suppresses vomiting response
- Antispasmodic
Tricyclic antidepressants (TCAs)

- **Action:** Block the reuptake of serotonin and norepinephrine, resulting in increased serotonin and norepinephrine in the synaptic cleft and subsequent down-regulation of the postsynaptic receptors.
Tricyclic antidepressants

- CATS:
  - Anxiolytic effect
  - Aggression
  - Compulsive Disorder
  - Urine spraying
  - Hypervocalization
Effects - Therapeutic

- **Norepinephrine**
  - ↓ General arousal
  - ↑ Attention
  - ↓ Mood reactivity
  - Stress response modulation

- **Serotonin**
  - Regulate mood states
  - ↓ Fear responses
  - Feeding behavior
  - ↓ Stress response
  - ↓ Impulsive behavior
Tricyclic antidepressants (TCAs)

- Side effects:
  - Sedating
  - Emesis and other GI upset
  - Lowers seizure threshold
  - Hypotensive
  - Urine retention
  - Dry mouth
  - Decreased tear production
  - May cause cardiac arrhythmias in humans.
Tricyclic antidepressants (TCAs)

- Bitter taste
- May require 3-4 weeks or longer to take full effect
Tricyclic antidepressants

- **Amitriptyline HCl (Elavil® & generic)**
  - Cheap but not very serotonin specific
  - Mainly used for its antihistaminic effects
  - More side-effects than the more serotonin-specific clomipramine

- **Clomipramine HCl (Anafrani®, Clomicalm™)**
  - Human generic used to be inexpensive
  - Now human generic is exorbitant in price
  - Clomicalm™ is still manufactured at 20 mg and 80 mg sizes. Generally less expensive to use Clomicalm™ than human generic
SSRIs

- Selective Serotonin Reuptake Inhibitors (SSRIs)
- May have 1-4 week+ latency to effect
- Long t1/2
- Action: Inhibition of serotonin reuptake. This increases serotonergic neurotransmission by allowing serotonin molecules to act for extended periods of time.
Selective Serotonin Reuptake Inhibitors (SSRIs)

- CATS:
  - Anxiolytic effect
  - Aggression
  - Compulsive Disorder
  - Urine spraying
  - Hypervocalization
Selective Serotonin Reuptake Inhibitors

- Side effects:
  - Anorexia/Hyporexia
  - Sedation
  - Gastrointestinal signs
  - Anxiety
  - Irritability
  - Insomnia
  - Aggression
Selective Serotonin Reuptake Inhibitors

- **Fluoxetine HCl** (Reconcile™, no longer manufactured, Prozac®)
  - Most commonly used SSRI in dogs and cats
  - Cost
  - Most information on its efficacy and side-effects, both published and unpublished

- **Paroxetine HCl** (Paxil®)
  - as for fluoxetine

- **Sertraline** (Zoloft®)
**Monoamine Oxidase-B Inhibitors**

- **Uses:** "**Cognitive dysfunction**" a.k.a. Alzheimer’s Disease

- **Selegiline HCl or L-deprenyl** (Eldepryl® (human), Anipryl® (canine))

- Not FDA approved for cats, but is used in cats extra-label
Monoamine Oxidase-B Inhibitors (MAOIs)

- Side effects:
  - Diarrhea
  - Restlessness
  - Salivation
  - Lethargy
  - Anorexia
Trazadone

- Serotonin receptor agonist and reuptake inhibitor
- Given “as needed” one to two hours before a stress-inducing situation
- Most common side effects
  - gastrointestinal effects (vomiting and diarrhea)
  - Sedation
  - ataxia
  - hypotension
  - excitement or agitation
  - panting.
Clonidine

- Alpha-2 agonist
- Given as needed
- Potential side effects
  - dry mouth
  - ataxia
  - constipation
  - sedation.
Buspirone (Buspar® & generic)

- 5-HT Agonist
- Dopamine D2 receptor antagonist
- Uses: Phobias, urine spraying, timid cats
- Side effects: Rare
  - Paradoxical anxiety
- Not sedating
- No potential for human abuse
Azapirones

- Must be given daily
- May require 1-3 weeks to take effect
- Anxioselective
- No anticonvulsant effects (Benzodiazepines are anxiolytics with anticonvulsant effects)
- No sedative or hypnotic effects
- No physical dependence (Contrast with Benzodiazepines)
Cats that have previously been timid in the face of repeated attacks may turn on their attacker. This can be beneficial or harmful, depending on the situation.
Azapiriones

- Many owners report that their cat becomes more “affectionate”, rubbing them, sitting in their lap and otherwise seeking contact with them for greater frequencies and durations.
Benzodiazepines

- Side Effects:
  - Sedation
  - Muscle relaxation
  - Increased appetite
  - Paradoxical excitation
  - Idiopathic hepatic necrosis in cats (diazepam/Valium)
Use with caution in fear aggression. Learned inhibition of aggression may be lost.

Withdraw gradually. Sudden termination in a patient that has been on for a long period of time can result in rebound, i.e. a resumption of symptoms which may be more intense than prior to treatment. In case of overdose:
Benzodiazepines

- **Diazepam** (Valium® & generic)
- **Clorazepate dipotassium** (Tranxene® & generic)
- **Alprazolam** (Xanax® & generic)
- **Oxazepam** (Serax® and generic)
Benzodiazepines

- Advantage is rapid onset of effect in treatment of anxiety.
- Potential for human abuse
- May or may not interfere with learning conditioned responses
Serotonin Syndrome: Overdose of serotonergic agents or certain combinations

I. Mental changes
II. Neuromuscular changes
III. Autonomic changes

- Usually mild and resolves in 24 to 72 hours
- Can cause death
- Mortality rate in humans of 11%
Pets with anxieties, phobias and compulsive disorder often have low serotonin function.

We give medications that facilitate the production, activity and/or retention of serotonin to correct this.

Serotonin Syndrome occurs when there is too much serotonin activity.
Symptoms reported in Humans

- Mental status
  - Confusion
  - Agitation
  - Coma
  - Hypomania
  - Anxiety

- Motor abnormalities
  - Myoclonus
  - Hyperreflexia
  - Muscle rigidity
  - Restlessness Tremor
  - Ataxia
  - Shivering
  - Nystagmus
  - Seizures
Symptoms reported in Humans

- Cardiovascular
  - Sinus tachycardia
  - Hypertension
  - Hypotension

- Gastrointestinal
  - Nausea
  - Diarrhea
  - Abdominal pain
  - Salivation
Serotonin Syndrome (SS)

- If suspected, contact the veterinarian immediately.
- While most cases of serotonin syndrome can be resolved by withdrawing all serotonin facilitating drugs and giving supportive care, SS can be fatal, so treat it as a life-threatening emergency.
Things relevant to the cat’s medication that the behaviorist can do to help

- Go over the instructions on the prescription with the owner to make sure that they understand. The prescription of psychoactive medications often involves steadily changing doses and, even if they thought they understood the instructions when going over them at the veterinarians, they may get confused later.

- The owner should have been provided written information on side-effects. Based on that material and your own knowledge of the drug, help the owner identify if any side-effects are occurring.

- Hopefully the medication will help, but changes are often slow and subtle, accumulating over time. Help the owner identify when any kind of improvement is occurring.