Psychotropic Agents

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Psychotropic Drugs

- How do we choose one drug over another?

Plan

- Use a similar type of experimental method to that used in human psychiatry
- need to have a good knowledge of the drugs available

Understand

- The agents that are available
- how they work or their general actions
- side effects
- therapeutic effects

Reasons for knowing the pharmacology

- So that you know the probable effects of the medication
- helps to distinguish if one product isn’t effective

- Determine the animal’s motivation
- characterise the signs that the medication will address
- identify a set of behavioural target signs

- These will act as indicators of the effectiveness of the pharmacological intervention
- diaries or video are an excellent tool
- need to know the time it takes for a drug to be effective

- " The treatment goals…..include significant and persistent reduction of target symptoms with as few side effects as possible" (Brandwein, 1993)

Pheromones

- Feliway - feline facial pheromone analogue
- DAP - Dog Appeasing Pheromone
- more effective if there is an underlying anxiety

Pheromones

- Thought to work by stimulating olfactory receptors
- can be used as a spray on objects or through a diffuser

Uses

- F3
  - indoor urine spraying
  - reduction of roaming from a new environment
  - improved food intake in hospitalised cats
- F4
  - reduces aggression in response to handling by strange people
  - reduce stress in a shelter

DAP uses

- Settling a new puppy in
- reducing fear
- helps to treat separation anxiety
- reduces travel sickness

Anxiolytics

- Benzodiazepines
- azapirones
- barbituates
- antihistamines

Benzodiazepines

- Activate benzodiazepine receptors in the CNS to facilitate GABA transmission
- GABA is an inhibitory neurotransmitter

Names

- Diazepam
- clorazepate
- alprazolam
- oxazepam
- lorazepam
- temazepam

Benzodiazepines

- Uses:
  - Fears, phobias and anxiety - dogs
  - urine spraying - cats
- rapid onset of action
- rapidly metabolised

Side Effects

- Soon after administration

- sedation
- ataxia
- muscle relaxation
- increased appetite
- paradoxical excitement
- memory deficits

Side Effects

- Over the first few days of treatment may develop tolerance to the sedation, ataxia and muscle relaxation
- caution in fearful animals since aggressive behaviour may be disinhibited

After Chronic Use

- Withdraw slowly to avoid discontinuation syndrome (recurrence of initial signs, nervousness and seizures)

- taper the dose by 25% per week until stopped

- Very well tolerated in dogs

- in cats idiopathic hepatic necrosis can occur within 7 days of starting treatment

- screen for liver function before start therapy and then one week later

- remember that BZs are subject to human abuse

Diazepam

- Effective in 55-75 % of cases of urine spraying
- possibly greater efficacy in males than females
- when medication is stopped relapse is common

- Hepatic necrosis can occur
- could be used in sporadic events in dogs

Alprazolam

- High potency BZ
- more rapid onset of action than diazepam
- fearfulness and phobias - dogs
- individual dosing important

Azapirones

- Antianxiety drug with serotonergic, noradrenergic and dopaminergic effects
- buspirone - partial seretonin-1alpha agonist
- used for generalised anxiety and to modulate states of high arousal - includes some feline spraying

- Improvement in 55% of cats
- 50% relapse rate following cessation of treatment
- may reduce intercat aggression when given to the more fearful individual

Buspirone

- Slow onset of action - 1-3 weeks
- side effects benign - GI signs, irritability, changes in social relationships including mild aggression in multicat households
- can have paradoxical increase in anxiety
- non-sedating

Antidepressants

- Tricyclic antidepressants
- selective serotonin reuptake inhibitors
- monoamine oxidase inhibitors

Tricyclic Antidepressants

- Block the uptake of serotonin (5HT) and noradrenaline

- Examples:
  - amitriptyline
  - imipramine
  - clomipramine

Uses

- In dogs
  - aggression
  - urine marking
  - repetitive behaviours
  - anxiety states

Uses

- In cats
  - certain forms of aggression
  - urine spraying
  - excessive grooming
  - anxiety states
  - excessive vocalisation

- May take 2-4 weeks before effect is seen
- commonly produce side effects due to their activity at muscarinic and antihistaminic sites
- mild sedation - common especially in the first week

Side Effects

- Anticholinergic effects -
  - dry mouth
  - urinary/ faecal retention

- antihistaminic effects
- cardiac conduction disturbances
- rarely may cause agranulocytosis
- may lower seizure threshold

TCAs

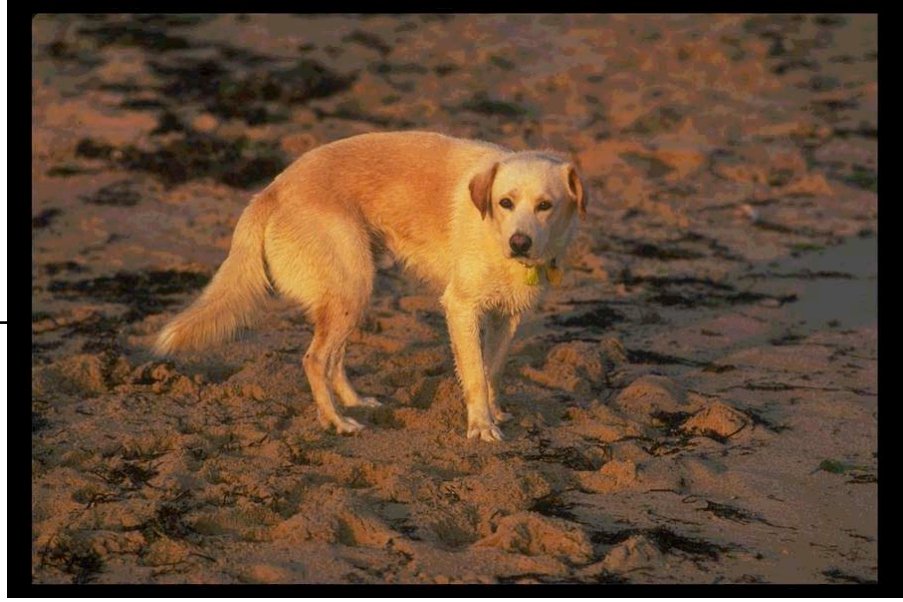
- Bitter - may cause hypersalivation
- competitively metabolised by phenothiazines

- metabolism stimulated by the concurrent use of barbituates
- Cimetidine may inhibit antidepressant metabolism

Amitriptyline

- Widely used to help behavioural therapy programmes
- enhances behavioural calming
- can be used alone or with pheromones

Amitriptyline



- cats -
  - urine spraying and inappropriate urination secondary to idiopathic cystitis
  - psychogenic alopecia
- dogs -
  - anxiety disorders
  - certain forms of aggression
  - repetitive self trauma

Clomipramine

- Predominantly affects serotonin
- obsessive-compulsive disorder - humans
- compulsive disorders - dogs
- anxiety disorders

Clomipramine

- Cats
  - compulsive disorders
  - spraying

Selective Serotonin Reuptake Inhibitors

- Block the reuptake of serotonin
  - fluoxetine
  - paroxetine
  - sertraline
- can be 3-4 weeks to onset
- may need 8 weeks or more to see maximal effects on compulsive disorders

SSRIs

- Dogs -
  - anxiety states
  - compulsive disorders
  - status-related aggression
- Cats -
  - anxiety disorders
  - urine spraying

SSRIs

- Monitor cat for water and food consumption, weight and elimination habits

Side Effects

- Gastrointestinal irritation
  - anorexia, inappetance, nausea or diarrhoea
- sedation
- insomnia
- irritability

- nearly no cardiovascular disturbances

Fluoxetine

- Widely used in humans
- 3-4 week latency to effect
- Dogs -
  - has been used for dominance aggression
  - compulsive disorders
- Cats -
  - urine spraying
  - compulsive disorders
  - anxiety states and aggression

Monoamine Oxidase Inhibitors

- Irreversible inhibitor of monoamine oxidase (an enzyme that catabolises noradrenaline, adrenaline, dopamine, tyramine and serotonin)
- Selegiline

Selegiline

- Canine cognitive dysfunction
- Feline cognitive dysfunction
- can have SERIOUS side effects when combined with some other drugs that affect neurotransmitter concentrations

Side Effects

- CNS toxicity and serotonin syndrome can occur if combined with SSRIs, non-specific MAOs or TCAs

- potentially fatal syndrome - increased BP, altered mental status, restlessness or hyperthermia, tremor

Side Effects

- Contraindicated - don’t use with alpha 2 agonists, phenothiazines and opiate analgesics

- do not use in pregnant or lactating animals

Antipsycotics

- Block dopamine receptors (among other things!)
  - acepromazine
  - haloperidol
  - chlorpromazine

Acepromazine

- Sedative neuroleptic
- has been used to non-specifically manage behaviour problems such as
  - noise phobia
  - aggression

- Reduces the animal’s awareness of environmental stimuli
- produces sedation
- other agents are now preferred since they are more specific

- Variable response to treatment and unacceptable side effects
- may provoke seizures, sedation, anticholinergic effects and extrapyramidal symptoms

Progestogens

- Widely used to suppress male-hormone dependant behaviours and may have tranquillizing effects
- non-specific in effect
- lots of side effects

- Not recommended as first line of treatment

Side Effects

- Side Effects include:
- hypercalcaemia
- polyphagia, polydipsia, polyuria decreased packed cell volume mammary nodules pyometra, diabetes mellitus, increased insulin levels, bone marrow suppression, increased growth hormone.

Xanthine Derivatives

- Propentofylline - reduces free radical generation and influences neuronal firing
- improves cerebral blood flow - vasodilatation
- increased cardiac output and RBC flexibility

- Treats a number of age related changes in dog behaviour

Management

- Followups are needed
- may need to make adjustments