Feline Pyschopharmacology: Medications for now and later

M. Leanne Lilly DVM DACVB

Low Stress Silver, Cat Friendly Veterinarian, Fear Free Elite & Shelter

Linkedin: mleannelilly

Psychopharmacology is becoming increasingly common as both clinician and clients recognize fear, anxiety, and stress in pets, and strive to address them. Doing so improves patient and client outcomes, increases safety, and improves quality of life. But where to start and how to choose? (All doses listed are for felines)

Medications for "now"
Adjunct/rapid acting which start working with-in minutes to hours, but also wear off in hours, starting with tools to send home:

Gabapentin: [5-50mg/kg Q8-12] a neuromodulator that has dose-dependent sedative and an adjunctive (but minimal) anti-seizure effect. Binds to the $\alpha_2\delta$ subunit on Ca^{2+} voltage gated channels, only when they are open. It is increasingly used to manage parasethesias, and neuropathic and chronic pain in a variety of species (cats(Guedes et al., 2018), dogs, etc.) though the data on this is still sparse and over prescribing is now a potential concern aside from it's potential for abuse. Has been well studied for stress-related to veterinary visits(Kruszka et al., 2021; Pankratz et al., 2017; van Haaften et al., 2017) Side effects include excess sedation, agitation, increased vocalization, or decreased appetite. It is predominantly cleared by the kidneys. *Liquid gabapentin for humans commonly contains xylitol, caution must be considered in scripting liquid out for feline households that contain dogs.*(American Veterinary Medical Association, 2017)

Benzodiazepines: true anti-panic medications which facilitate GABA binding to the GABA A receptor. The potential side effects are hyperactivity, hyperexia, increased aggression, ataxia, and vomiting and diarrhea. They are selected based on duration needed and metabolism. Alprazolam (2-4 hrs), and lorazepam (8-12+). They are all metabolized by the liver, the least so lorazepam which is glucuronidated to a non-active metabolite. Diazepam may case fulminant hepatic necrosis in cats when given PO(Center et al., 1996; Hughs et al., 1996); both clorazepate and chlordiazepoxide share the entire metabolic pathway with diazepam so are best avoided in cats. *Due to the risk of disinhibition, agitation, these are less frequently used. Additionally, there is the risk for abuse and diversion problems.*

Trazodone: [50-100mg/cat 90+ minutes prior to event] a serotonin antagonist reuptake inhibitor (SARIs). It antagonizes the auto-receptor, so it's convenient to think of it as having the same overall effect of an SSRI without the 4 to 6-week lag time. It also has an antihistamine property that can have a calming effect. Onset time of action appears variable in cats, ranging from 60 minutes to 3 hours(Orlando et al., 2016; Stevens et al., 2016) It is metabolized by the liver, cleared by the kidneys, has been documented in healthy cats to decrease systolic blood pressure with no echocardiographic or heart rate changes.(Fries et al., 2019)

Acepromazine: [0.1-2.2mg/kg PO, IM, SQ] a phenothiazine sedative hypnotic related to typical anti-psychotics. This medication inhibits dopamine in the nigrostriatal pathway effectively inhibiting movement. It has not been shown to have any primary anxiolytic properties, and may worsen anxiety or fear when used as sole agent.(Seibert, Lynne and Crowell-Davis, 2019)

Buprenorphine injectable [0.02-0.04 mg/kg TM can send home or use in clinic, 0.01-0.02mg/kg IM, IV in clinic](KuKanich and Papich, 2017) this is a "mixed agonist", a partial μ agonist, with high affinity, and an antagonist at the κ opioid receptor. This mixed action gives it better safety profile that a pure μ agonist, and in cats produces less dysphoria, excitement, vomiting or nausea. While the sedative effects may last for 2-6+ hours, the analgesic effects of formulations other than Simbadol™ last around 4 hours, but it's metabolites may have analgesic effects. It has reasonable bioavailability (30%) through the mucous membranes, but has poor true oral bioavailability (~10%) so getting it on the gums or in the buccal pouch is key for at home or in hospital administration. Zorbium may also work very quickly, but does last for 4 days.

Oral combinations there are no studies on combinations

- **o** Trazodone and gabapentin
- **o** Lorazepam and acepromazine*
- **o** Gabapentin and acepromazine*
- o Gabapentin and lorazepam
- o Gabapentin + buprenorphine
- o Lorazepam + buprenorphine
- o Gabapentin + acepromazine* + buprenorphine

*Patients with pre-existing anxieties and fears are more likely to 'fight' through medication, acepromazine should only be used in combination with other oral medications, even if pet is on a long lasting medication (SSRI, TCA)

Butorphanol injectable (Torbugesic) [0.1-0.4mg/kg IM, IV, SC OTM]. This is another mixed agonist with likely the reverse actions of buprenorphine (κ agonist, and either partial agonist or antagonist at μ receptors). This may explain why experientially it provides more sedation, but less analgesia, and its propensity for being far less emetic than morphine, and in some reports buprenorphine. It is cleared far more slowly by cats than dogs, giving it a half life roughly equivalent to buprenorphine, with analgesia lasting ~2.5-3 hours.(KuKanich and Papich, 2017)

Dexmedetomidine injectable (Dexdomitor)(Zoetis Inc., 2015) **[**10-40μg/kg IM or OTM] an α_2 agonist routinely used for sedation, due to it's increased specificity for auto-receptors in the CNS, slowing the release of norepinephrine to decrease anxiety and at most used doses, overall activity. Cats seem to be particularly sensitive to emetic effects and this is worse with OTM than injection, and as a solo agent.(Porters et al., 2014; Santos et al., 2010; Slingsby et al., 2009) Because of the propensity for bradycardia and hypotension, this should be avoided in cardiovascular disease, or combination with other hypotensive, but it can be reversed with Antisedan (atipamazole).

Ketamine (Ketaset) [1-5mg/kg IM(Donald C. Plumb, 2015) or OTM- caution, BITTER] an NMDA antagonist dissociative and general anesthetic. Most practitioners are familiar with ketamine as part of 'kitty magic' (dexdomitor, ketamine, and an opioid) or in combination with diazepam for induction. However it can also be utilized as part of an OTM protocol at similar doses but with lesser effect due to lower bioavailability. Where this may be most useful is a cat whose mouth we can access through a kennel door during hissing, but who cannot be otherwise safely handled for an injection.

Midazolam (Versed)(Donald C. Plumb, 2015) [0.2-0.4mg/kg IM, IV] an injectable benzodiazepine. It can cause respiratory compromise and disinhibition of aggression. This is most common in already agitated or profoundly panicked patients and should consequently rarely if ever be used as a single agent for highly aroused patients. Appetite increase, muscle relaxation, and ataxia may also be seen. Can be reversed with flumazenil but few practices carry this.

Telazol (tiletamine/zolazepam) [5-10mg/kg IM, 5-7.5mg/kg OTM] a combination of an NMDA antagonist dissociative anesthetic with a benzodiazepine. The zolazepam will wear off first leaving most patients with a dissociative state that lasts longer(2-4+ hours) than functional sedation (30-60 minutes). It is implicated in pancreatitis so should be avoided or used with significant caution in patients with a history of pancreatic disease or respiratory compromise. It can be combined with α_{2s} or acepromazine for particularly fractious patients or in end of life situations. Despite the label for dogs, it is NOT FDA approved for IV induction of anesthesia in cats, though has been used for sedation in the buccal pouch. It will decrease respiratory and heart rates as well as systolic pressure with this use as well.

Injectable combinations

Young, healthy, fractious feline:

Dexmedetomidine 10-20μg/kg + butorphanol 0.2-0.4mg/kg + 2-5mg/kg ketamine IM
Telazol 5-7.25mg/kg OTM followed by dexmedetomidine 5-10mcg/kg + butorphanol 0.2-0.4mg/kg IM

Geriatric fractious cat

Dexmedetomidine 5μg/kg + butorphanol 0.2-0.4mg/kg
OR acepromazine 0.05mg/kg + butorphanol 0.2-0.4mg/kg

Geriatric/debilitated fearful <u>not</u> fractious cat

Midazolam 0.2-0.4mg/kg + butorphanol 0.2-0.4mg/kg ± acepromazine 0.05mg/kg IM

Medications for Later:

Daily medications ('for later') which may take as long as 6 weeks for full effect, but provide 24-7 'coverage' at steady state. Do not use with MAOI (Amitraz) containing flea/tick products.

SSRIs

Fluoxetine (Prozac/ Reconcile): [0.5-1.5mg/kg PO Q24], most effective for urine marking in cats(Hart et al., 2005). May take up to 6 weeks to see full effect. The most common side effects are decreased appetite, sedation. Less common side effects include other GI effects, increased anxiety, and changes in platelet function (increased risk of bleeding). Hepatic metabolism into active metabolites with long half-lives. Renal clearance.(Ogata et al., 2019)

Sertraline (Zoloft) [0.5-1.5mg/kg PO Q24] not labeled for cats, no placebo controlled trials. Case report of use for FIC and marking.(Lilly, 2020) Least sedating, hepatically metabolized and mostly enterically cleared.(Ogata et al., 2019) Almost always requires custom compounding for appropriate dosing.

Paroxetine (Paxil) [0.5-2mg/kg Q12 K9; 0.5-1mg/kg Q24 feline] not labeled for cats, but many report using it for compulsive behaviors, or generalized anxiety(Landsberg et al., 2013) as well as urine marking, and aggression(Ogata et al., 2019). Mild increase in appetite and anticholinergic side effects can be problematic for use in cats with lower urinary tract signs especially. Hepatic metabolism, renal clearance.

SNRI

Venlafaxine (Effexor): [0.5-2mgk/kg Q24] In 176 retrospective, 90% of owners and veterinarians reported improvements across fears, aggression and housesoiling. (Masson et al., 2025). Has also been used in a case series in FIC(Hopfensperger, Marie J., 2016). Side effects are consistent with SSRIs, hepatic metabolism, renal clearance (we think).

TCAs

Clomicalm (clomipramine):[0.25-2mg/kg Q24](Crowell-Davis, 2019; Denenberg, 2020) **s**tudied in cats for urine marking(Hart et al., 2005; Landsberg and Wilson, 2005) and used for self trauma(Amengual Batle et al., 2019) and compulsive disorders.(Seksel and Lindeman, 1998) Roughly 3-5 weeks to see anti- anxiety effects. Side effects may include gastrointestinal upset (vomiting or diarrhea), changes in appetite, sedation, increased anxiety or aggression, and anti-cholinergic side effects are common.(Crowell-Davis, 2019) Unlike in dogs, no EKG changes have been found, but euthyroid decrease in T4 are seen(Martin, 2010)

Amitriptyline (Elavil) [0.5-1mg/kg Q24] less serotonergic than Clomicalm, more anti-histaminic. Roughly 3-5 weeks to see anti- anxiety effects. same side effect profile as Clomicalm, except thyroid suppression.(Crowell-Davis, 2019)

OTHERS

Buspirone (Buspar) [0.5-1mg/kg Q12] azapirone serotonin agonist, non-sedating. Colloquially termed the "bravery drug," Though very rare, side effects include mild sedation, agitation, gastrointestinal upset, and increased aggression. Increased friendliness toward humans has been reported.(Dantas and Crowell-Davis, Sharron L, 2019a)

Selegiline (Anipryl) [0.25-1mg/kg Q24](Gunn-Moore, 2011) a reversible monoamine oxidase inhibitor intermittently available in US as non-generic. Labeled for Canine Cognitive Dysfunction to give in the morning, with some increasing use in Feline Cognitive Dysfunction(Dehasse, 1999; Landsberg et al., 2010). GI upset, agitation most common side effects. Hepatically metabolized, renally cleared. *Risk of interaction with any other moderately serotonergic medication- trazodone, tramadol, SSRI, buspirone, trazodone etc.*(Dantas and Crowell-Davis, Sharron L, 2019b)

We will discuss some case examples in an interactive format, including anesthetic considerations.

References:

Amengual Batle, P., Rusbridge, C., Nuttall, T., Heath, S., Marioni-Henry, K., 2019. Feline hyperaesthesia syndrome with self-trauma to the tail: retrospective study of seven cases and proposal for an integrated

multidisciplinary diagnostic approach. Journal of Feline Medicine and Surgery 21, 178–185. https://doi.org/10.1177/1098612X18764246
American Veterinary Medical Association, 2017. Eliminate xylitol from canine prescriptions [WWW Document]. American Veterinary Medical Association. URL https://www.avma.org/blog/eliminate-xylitol-canine-prescriptions (accessed 8.25.21).
Center, S.A., Elston, T.H., Rowland, P.H., Rosen, D.K., Reitz, B.L., Brunt, J.E., Rodan, I., House, J., Bank, S., Lynch, L.R., Dring, L.A., Levy, J.K., 1996. Fulminant hepatic failure associated with oral administration of diazepam in 11 cats. J. Am. Vet. Med. Assoc. 209, 618–625.
Crowell-Davis, S.L., 2019. Tricyclic Antidepressants, in: Veterinary Psychopharmacology. Wiley-Blackwell, Hoboken, NJ, pp. 231–256.
Dantas, L.M. de S., Crowell-Davis, Sharron L, 2019a. Miscellaneous Serotonergic Agents, in: Veterinary Psychopharmacology. Wiley-Blackwell, Hoboken, NJ, pp. 129–146.
Dantas, L.M. de S., Crowell-Davis, Sharron L, 2019b. Monoamine Oxidase Inhibitors, in: Veterinary Psychopharmacology. Wiley-Blackwell, Hoboken, NJ, pp. 185–190.
Dehasse, J., 1999. The use of selegiline in cat behavioural pathologies.
Denenberg, S. (Ed.), 2020. Small animal veterinary psychiatry, 1st ed. CAB International, Boston.
Donald C. Plumb, 2015. Plumb's Veterinary Drug Handbook, 7th ed. PharmaVet, Stockholm, Wisconsin.
Fries, R.C., Kadotani, S., Vitt, J.P., Schaeffer, D.J., 2019. Effects of oral trazodone on echocardiographic and hemodynamic variables in healthy cats. Journal of Feline Medicine and Surgery 21, 1080–1085. https://doi.org/10.1177/1098612X18814565
Guedes, A.G.P., Meadows, J.M., Pypendop, B.H., Johnson, E.G., Zaffarano, B., 2018. Assessment of the effects of gabapentin on activity levels and owner-perceived mobility impairment and quality of life in osteoarthritic geriatric cats. Journal of the American Veterinary Medical Association 253, 579–585. https://doi.org/10.2460/javma.253.5.579
Gunn-Moore, D.A., 2011. Cognitive Dysfunction in Cats: Clinical Assessment and Management. Topics in Companion Animal Medicine, Nutrition, Geriatrics and Behavior 26, 17–24. https://doi.org/10.1053/j.tcam.2011.01.005
Hart, B.L., Cliff, K.D., Tynes, V.V., Bergman, L., 2005. Control of urine marking by use of long-term treatment with fluoxetine or clomipramine in cats. Journal of the American Veterinary Medical Association 226, 378–382. https://doi.org/10.2460/javma.2005.226.378
Hopfensperger, Marie J., 2016. Use of oral venlafaxine in cats with feline idiopathic cystitis or behavioral causes of periuria.
Hughs, D., Moreau, R.E., Overall, K.L., Winkle, T.J.V., 1996. Acute Hepatic Necrosis And Liver Failure Associated With Benzodiazepine Therapy In Six Cats, 1986–1995. Journal of Veterinary Emergency and Critical Care 6, 13–20. https://doi.org/10.1111/j.1476-4431.1996.tb00030.x
Kruszka, M., Graff, E., Medam, T., Masson, S., 2021. Clinical evaluation of the effects of a single oral dose of gabapentin on fear-based aggressive behaviors in cats during veterinary examinations. javma 1–7. https://doi.org/10.2460/javma.20.06.0307
KuKanich, B., Papich, M.G., 2017. Opioid Analgesic Drugs, in: Veterinary Pharmacology and Therapeutics. Wiley-Blackwell, Hoboken, NJ, pp. 165–449.
Landsberg, G.M., Denenberg, S., Araujo, J.A., 2010. Cognitive Dysfunction in Cats: A Syndrome we Used to Dismiss as 'Old Age.' Journal of Feline Medicine and Surgery 12, 837–848. https://doi.org/10.1016/j.jfms.2010.09.004
Landsberg, G.M., Hunthausen, W.L., Ackerman, L.J., Fatjó, J., 2013. Pharmacologic intervention in behavior therapy, in: Behavior Problems of the Dog and Cat. Saunders Elsevier, Edinburgh, pp. 113–138.
Landsberg, G.M., Wilson, A.L., 2005. Effects of clomipramine on cats presented for urine marking. J Am Anim Hosp Assoc 41, 3–11. https://doi.org/10.5326/0410003
Lilly, M.L., 2020. Animal Behavior Case of the Month. Journal of the American Veterinary Medical Association 257, 493–498. https://doi.org/10.2460/javma.257.5.493
Martin, K.M., 2010. Effect of clomipramine on the electrocardiogram and serum thyroid concentrations of healthy cats. Journal of Veterinary Behavior 5, 123–129. https://doi.org/10.1016/j.jveb.2009.12.019

Masson, S., Metz, D., Bleuer-Elsner, S., Schwobthaler, F., 2025. Retrospective study on the use of venlafaxine in 176 cats diagnosed with behavioral disorders. Journal of Veterinary Behavior 77, 1–10. https://doi.org/10.1016/j.jveb.2024.11.004

Ogata, N., Dantas, L.M. de S., Crowell-Davis, S.L., 2019. Selective Serotonin Reuptake Inhibitors, in: Veterinary Psychopharmacology. Wiley-Blackwell, Hoboken, NJ, pp. 103–128.

Orlando, J.M., Case, B.C., Thomson, A.E., Griffith, E., Sherman, B.L., 2016. Use of oral trazodone for sedation in cats: a pilot study. Journal of Feline Medicine and Surgery 18, 476–482. https://doi.org/10.1177/1098612X15587956

Pankratz, K.E., Ferris, K.K., Griffith, E.H., Sherman, B.L., 2017. Use of single-dose oral gabapentin to attenuate fear responses in cage-trap confined community cats: a double-blind, placebo-controlled field trial. J. Feline Med. Surg. https://doi.org/10.1177/1098612X17719399

Porters, N., Bosmans, T., Debille, M., de Rooster, H., Duchateau, L., Polis, I., 2014. Sedative and antinociceptive effects of dexmedetomidine and buprenorphine after oral transmucosal or intramuscular administration in cats. Veterinary Anaesthesia and Analgesia 41, 90–96. https://doi.org/10.1111/vaa.12076

Santos, L.C.P., Ludders, J.W., Erb, H.N., Basher, K.L., Kirch, P., Gleed, R.D., 2010. Sedative and cardiorespiratory effects of dexmedetomidine and buprenorphine administered to cats via oral transmucosal or intramuscular routes. Veterinary Anaesthesia and Analgesia 37, 417–424. https://doi.org/10.1111/j.1467-2995.2010.00555.x

Seibert, Lynne, Crowell-Davis, S.L., 2019. Antipsychotics, in: Veterinary Psychopharmacology. Wiley-Blackwell, Hoboken, NJ, pp. 201–215.

Seksel, K., Lindeman, M., 1998. Use of clomipramine in the treatment of anxiety-related and obsessive-compulsive disorders in cats. Australian Veterinary Journal 76, 317–321. https://doi.org/10.1111/j.1751-0813.1998.tb12353.x

Slingsby, L.S., Taylor, P.M., Monroe, T., 2009. Thermal antinociception after dexmedetomidine administration in cats: a comparison between intramuscular and oral transmucosal administration. Journal of Feline Medicine & Surgery 11, 829–834. https://doi.org/10.1016/j.jfms.2009.03.009

Stevens, B.J., Frantz, E.M., Orlando, J.M., Griffith, E., Harden, L.B., Gruen, M.E., Sherman, B.L., 2016. Efficacy of a single dose of trazodone hydrochloride given to cats prior to veterinary visits to reduce signs of transport- and examination-related anxiety. Journal of the American Veterinary Medical Association 249, 202–207. https://doi.org/10.2460/javma.249.2.202

van Haaften, K.A., Forsythe, L.R.E., Stelow, E.A., Bain, M.J., 2017. Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination. Journal of the American Veterinary Medical Association 251, 1175–1181. https://doi.org/10.2460/javma.251.10.1175

Zoetis Inc., 2015. Dexdomitor Package Insert. Kalamazoo, MI.