

1 **Feline Psychopharmacology**
Medications for Now & Later

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Pronouns: she/her/hers

2 **Psychopharmacology**

- Use of psychoactive* medications
 - Facilitate behavior modification
 - Decrease fear, anxiety
 - Restraint/sedation
- Improving quality of life

3 **When to consider psychoactive meds?**

- Severity of symptoms (fear/phobia/anxiety)
- Frequency, predictability of triggers
 - High frequency
 - Low predictability
 - High intensity of stimuli
- Behavior modification is unsuccessful
 - Insufficient progress vs effort/time
 - Pet too stressed to eat
- Risk of rehome/euthanasia

4

5

6 **Medications “For Now”**

- Often referred to as ‘adjunct’
- Start working within 20-120 minutes
- Wear off in 2-12 hours
- ± combined with each other
- ± with supplements/diets
- ± with longer lasting medications

7 **Medications “For Now”**

- Gaba analogue
- Benzodiazepines
- Serotonin antagonist/reuptake inhibitor
- α_2 agonists
- Phenothiazine
- Opioids

8 **Gabapentin**

- $\alpha_2\delta$ -1 Ca^{2+} ligand neuromodulator
- 10-50mg/kg Q8-12 Feline
- 88.7% bioavailable, $T_{1/2}$ 177 minutes
- Side Effects: sedation, GI side effects rare, weight gain? disinhibition of vocalization
- Renal clearance
- Human liquid gabapentin often contains *xylitol*
–Caution in households containing dogs

9 **Gabapentin**

- Disinhibition of vocalization
–Dose dependent
–Rare:
 - 4 cases between myself and close colleagues in 11 years
- Haven't yet seen in cats

10 **Gabapentin**

- 20 osteoarthritic cats with signs on PE & CSOM
–10mg/kg vs placebo Q12 x 2 weeks, then cross over
–Evaluated weekly
- Decrease overall activity, improved OA-impaired activities
- Client did not note QOL change until gaba removed
 - AE: sedation, ataxia, weakness, muscle tremor, lethargy

11 **Gabapentin**

- 50mg/cat (n=17)
- 100mg/cat (n=17)
–9.2-47.6 mg/kg
- Placebo (n=19)
- Decreased stress score, respiratory rate
- No global sedation score difference
- No adverse events

12 **Gabapentin**

- N=20, placebo controlled cross-over
- 2 vet visits 1 week apart
–1 with placebo, 1 with 100mg gabapentin (13.0-29.4 mg/kg)
- PE, BP
- Owner reported improved handling and pre-visit stress with gabapentin
- Masked-Veterinarian assessment concurred
- AE: Vomiting, ataxia, hypersalivation reported

13 **Gabapentin**

- N= 55 (26 with fear-related aggression at vet)
- Placebo controlled, double blinded
- 100 (7kg) or 200mg (> 7kg)
- 9 step standardized exam

- Measured exam compliance

14 **Gabapentin**

- FRA cats were less compliant pre-gabapentin than non FRA cats
- W/gabapentin no difference between FRA and non-FRA cat scores
- 77% of FRA cats ↓ scores
 - 23% the same, non worsened
- 35% drowsy, 23% myorelaxation, 11.5% ataxic, 1 cat vomited

15 **Benzodiazepines**

- GABA_A agonist true anti-panic medications
 - Diazepam= typical gold standard in lab-trials
- Side effects:
 - + Sedation, appetite stimulation
 - Aggression, paradoxical agitation/hyperness, ataxia, vomiting, diarrhea
- Hepatic metabolism; many of the metabolites are active

16 **Choosing a Benzodiazepine**

- Alprazolam (2-4 hrs)
- Diazepam (4-6)
- Clorazepate** (6-12)
- Lorazepam (8-12) least hepatic metabolism
- Clonazepam & chlordiazepoxide* (8-12+ hrs)

*share the entire metabolic pathway with diazepam

* Harder to find, and \$\$\$\$

17 **Diazepam**

- PO Associated with fulminant hepatic necrosis in cats (Hughs, 1996)
 - First 13 days of therapy
- Since 1996, 2 published case reports of surviving cats
 - 1/11 survived in second case series (Center, 1996)
 - 1 in 2012
 - 5 days in ICU (plasma transfusion, crystalloids, hetastarch, pentastarch, potassium supplementation, spironolactone, lactulose, vitamin K, N-acetylcysteine, S-adeosylmethionine, metoclopramide CRI, famotidine, NG tube, warming)

18 **Alprazolam**

- Duration of action 2-4 hours
- Dose schedule Q6
- Experientially see paradoxical responses on onset, throughout, or just at off set

19 **Lorazepam**

- Lasts 8-12 hours
- Very well tolerated in cats
- 0.125-0.25mg/ cat or 0.03-0.08mg/kg Q12
- Minimal hepatic metabolism

20 **Trying Benzodiazepines**

- Test without stressor first!

- May have to test without other stimuli as well (kids, other cats, dogs, food)
- Response to one benzo does NOT predict response to others
- If using around the clock or regularly (once daily for 2 weeks) decrease slowly
 - 25% per week

21 **Trazodone**

- Serotonin antagonist/ reuptake inhibitor (SARI)
- 50-100mg/cat (Orlando 2016)
- Anti-histamine effect may cause drowsiness
- Side effects: GI upset, worsening of pre-existing incontinence, lower seizure threshold
- less likely: agitation
- Priapism hasn't been documented in cats
- Hepatic metabolism, renal clearance

22 **Trazodone**

- N= 6
- 83%, 46% and 66% reduction in accelerometer activity after 2 hours
- Peak sedation ranged 1-3.0hr
 - McCune's cat stress scale pre-exam, exam (90 min), post exam
 - No difference in stress score between 100mg and placebo
- No Δ PE or Lab results

23 **Trazodone**

- N= 10
- 50mg/ cat
- 50, 75, 100mg / cat vs placebo
- Cross over with PE with placebo vs trazodone 3 weeks apart
- Ease of transport \uparrow (no stats due to low #s)
- Veterinarian + owner scale for handling ease \uparrow
- No Δ in PE variables
- 1 cat was sleepy, no other behavioral changes
- No no v/d

24 **α_2 Agonist: Clonidine**

- ~90 minutes to take effect
- 5-10 μ g/kg cats Q12 (Washabau, 2000)
- Side effects: low blood pressure, GI upset
- Hepatic metabolism (CYP2D6), renal clearance
- Contraindications: cardiovascular disease
- Caution with acepromazine, other hypotensives
- TCAs may decrease anti-hypertensive effects

25 **Phenothiazine (Acepromazine)**

- Sedative hypnotic
 - Inhibits DA in nigrostriatal motor pathway
 - Higher doses are dissociative
- 0.1-2.2mg/kg SQ/IM/PO
- Facilitates restraint, decreases MAC, anti-emetic, decreases urethral tone
 - No anxiolytic effects in peer reviewed literature

- May worsen anxiety as solo agent
- IN Combination for pets who are a danger to themselves or others

26 **Opioid: Buprenorphine**

- partial μ agonist, high affinity κ antagonist
- 0.02-0.04mg/kg TM
 - (0.01-0.02IM/IV in clinic; Simbadol 0.24 mg/kg SQ)
- 30% bioavailable TM (~10% oral)
- Side effects: sedation/analgesia, anorexia, tachycardia, hyperthermia; excitation more common with Simbadol than TM
- Hepatic metabolism (CYP3A4), renal clearance
- Contraindications: cardiovascular disease
- Caution with 3A4 substrates/inhibitors

27 **Picking a medication for “now”**

- How much warning will client have for ‘event’?
- How long will event last?
- How easy/safe is it to medicate my patient?
- Concurrent medical conditions/factors?
- Concurrent household factors*
- Test without stressor first!

28 **Medication for now ex:**

- 1 • 4 year old FS DSH
 - Hides for 24hrs after visitors, scratches and meows behind closed doors
 - CBC/Chem/T4 wnl
 - Want to have 40th b-day party ~4 hours
 - RX options?
 - Gabapentin
 - Lorazepam
 - Trazodone
- 2 • *Instead...*
 - History of well controlled seizures
 - RX option?
 - Gabapentin
 - Lorazepam

29 **Medication for now ex:**

- 1 • 3 year old MN DSH
 - Panics for fireworks, tries to climb into o’s clothes
 - CBC/Chem/T4 wnl
 - RX options?
 - Gabapentin
 - Lorazepam
 - Trazodone
- 2 • *Instead...*
 - Add on history of FIC episodes post fireworks resulting in urethral plug
 - RX option?
 - Gabapentin

- Lorazepam
- ± Buprenorphine?
- ± Acepromazine?

30 **Opioids and Behavior Medications**

- Fentanyl patches minimize 1st pass metabolism
- Methadone highest Q-T prolongation capacity
- Oxycodone dose dependent Q-T prolongation
 - Amitriptyline prolongs Q-T in K9
- Morphine cardioprotective rats, lowest fibrillation rate humans
 - Histamine release ☹
- Hydromorphone: no QT prolongation
 -

31 **Putting it together- Oral Combinations**

- Gabapentin + acepromazine*
- Gabapentin + trazodone
- Gabapentin + lorazepam
- Gabapentin + buprenorphine
- Lorazepam + acepromazine*
- Lorazepam + buprenorphine
- Gabapentin + acepromazine* + buprenorphine
- Gabapentin + lorazepam + acepromazine + buprenorphine

32 **When Oral Medications Are Not Enough...**

- The patient is too stressed/fearful/fractious
- The procedure is too painful/ you would sedate a non behavior patient
 - Pelvic-rads, laceration repair, oro-pharyngeal evaluation etc.
- Anesthesia is the goal 'anyway'
 - Dental cleaning, neutering, orthopedic/soft tissue surgery etc.
- Injectable sedation/chemical restraint

33 **Injectable Sedation/Chemical Restraint**

- Facilitates transition from oral to anesthesia
 - Facilitate procedure when oral meds are not enough
- IM preferred (vs SQ)
 - IV in rare cases
- Oral-Transmucosal (OTM) when not safe to inject
 - Requires higher doses
 - Takes 45-75 min to take effect
 - Some agents are bitter

34 **Sedation/Anesthesia of Behavior Patient**

- Patients not on long lasting medications should NOT skip am dose
 - Leads to rebound anxiety
- Fasted patients (planned anesthesia) can coat the pills in tiny amount of food
 - Not associated with increased risk of aspiration

35 **Butorphanol ('Torb'/Torbugesic™)**

Dose	0.1-0.4mg/kg IM, IV, or SC
Class	opioid partial agonist
Mechanism	Partial agonist/antagonist at μ and κ receptors
Onset	3 minutes IV, 15 minutes IM, SC; 45-60 OTM
Duration	1-4 hours
Contraindication	Severe renal insufficiency, severely disabled patients
Drug interactions	Other CNS depressants, will partially reverse a pure μ opioid
Side Effects	Sedation, mild bradycardia, respiratory suppression, mild ataxia
Comments	Pure μ opioids will provide better analgesia

36 **Dexdomitor™ (Dexmedetomidine)**

Dose	10-40mcg/kg IM or OTM
Class	α_2 agonist very specific for auto-receptors in CNS
Mechanism	Slows release of NE in brain, decreases anxiety
Onset	5-20 min IM, 45-60min OTM
Duration	45-60 min
Contraindication	CV disease, severe renal disease
Drug interactions	Hypotensives, other CNS depressants
Side Effects	VOMITING Bradycardia, vasoconstriction, hypothermia, pale/ashy mucous membranes, respiratory depression; \pm decrease in urine concentration
Comments	Gag reflex remains intact; can be reversed with half to equal volume atipamizole for IM, 1/3 -1/2 for OTM

37 **Ketamine (Ketaset™)**

Dose	1-5mg/kg IM
Class	Dissociative general anesthetic
Mechanism	NMDA antagonist
Onset	5-10 minutes
Duration	1 hour+
Contraindication	Hypertensive patients, congestive heart failure, caution in epileptics
Drug interactions	Other CNS depressants
Side Effects	Anesthesia, respiratory depression, seizures, dysphoria, myoclonus
Comments	Not used as a solo agent; stings. Keep closest to plunger, don't mix

38 **Midazolam (Versed™)**

Dose	0.2-0.4 mg/kg IM or IV
Class	Benzodiazepine
Mechanism	Potentiates GABA
Onset	3-5 minutes

Duration	1-2 hours
Contraindication	Severe respiratory compromise, aggressive patients
Drug interactions	Other CNS depressants
Side Effects	Likely: increased appetite, sedation, muscle relaxation; Possible: ataxia, aggression, paradoxical excitation
Comments	Best in combination

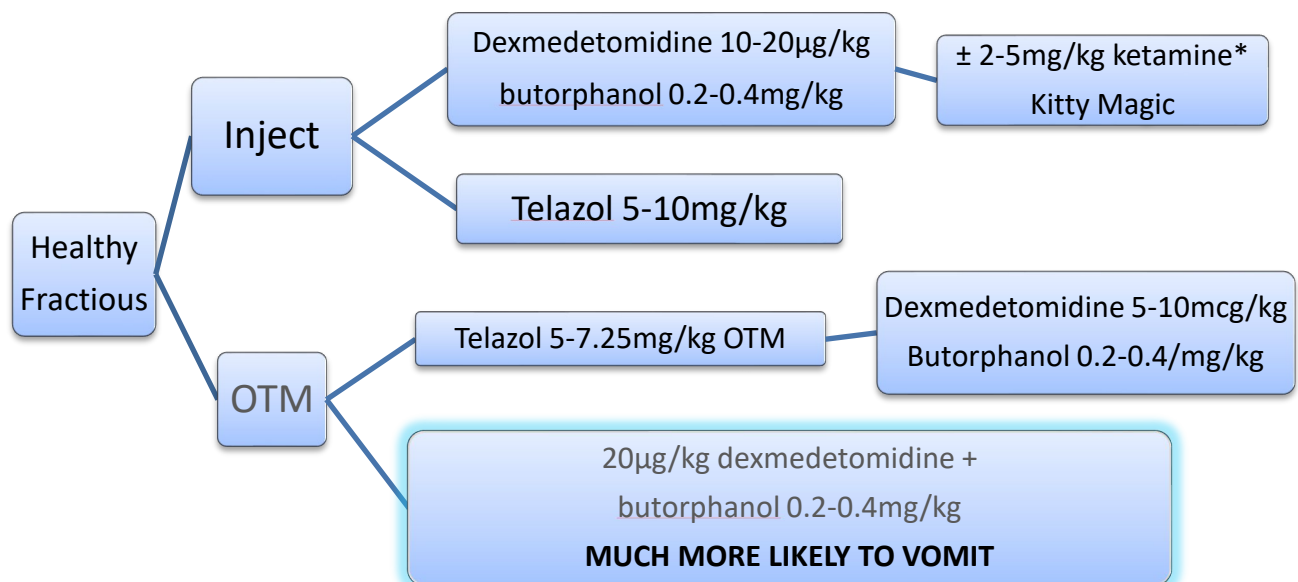
39 Telazol™ (Tiletamine/ zolazepam)

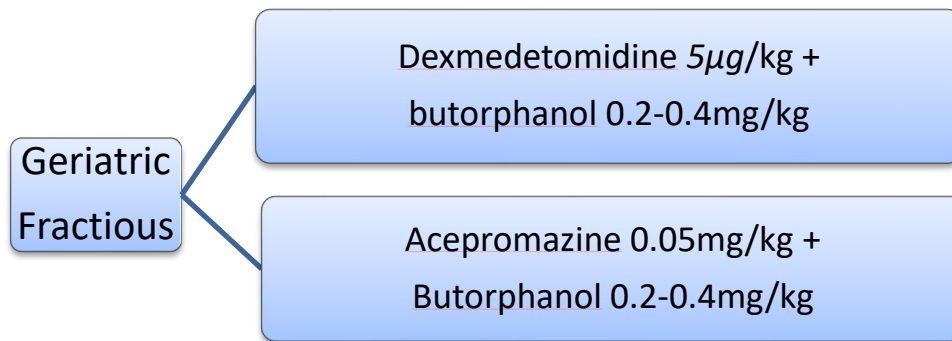
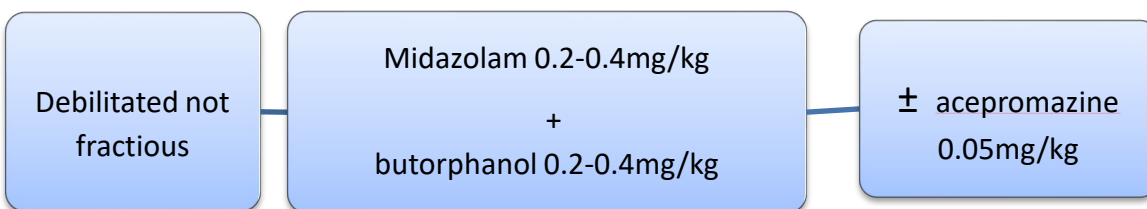
Dose	5-10mg/kg IM* 5-7.5mg/kg OTM
Class	Dissociative anesthetic/ benzodiazepine
Mechanism	NMDA antagonist / potentiates GABA
Onset	3-5 minutes
Duration	30-60 min*
Contraindication	Pancreatic disease, severe cardiac or respiratory compromise
Drug interactions	Other CNS depressants, may decrease efficacy of phenobarbital/phenytoin
Side Effects	Cardiac & respiratory depression, jerky recovery due to differing half-lives, less than ketamine alone
Comments	Lingering drowsiness often lasts much longer but not surgical plane. Readily combined with opioids

40 Alfaxalone

- Neurosteroid injection agent
- Linear kinetics, higher dose= longer sedation
- "IM Propofol"
- No analgesia
- Bottles with preservative can NOT be mixed with other medications
- Large volume for anything larger than ~5kg
 - Injection challenge for fractious pets

41 Creating cocktails for kitties



42 **Creating cocktails for kitties**43 **Creating cocktails for kitties**44 **Once Injected**

- Dark!
- Quiet!
- Wait to check or create system for client to alert you
 - Paper under door, sticker on the window etc.
- Every time you rouse the patient, you risk not being able to proceed
 - Inform clients they should be calm, quiet, gentle petting if anything

45 **Recovery**

- Quiet room, often dark-ish is useful
- Typically with client, sometimes as pet is extubated
- Place any needed equipment (cone, muzzle, bandages, slings, harnesses) prior to recovery/reversal
- Calming cap/blanket, cotton in ears may be helpful to smooth recovery
 - Who will remove those items and when?

46 **Opioids and Behavior Medications**

- Codeine, oxycodone CYP2D6 substrates
 - So are amitriptyline, clomipramine, paroxetine
 - Inhibitors: Fluoxetine, paroxetine, sertraline
- Pro-opioids (hydrocodone and codeine) less likely to control pain for patients on SSRIs
- Sedating effects may compound each other
 - Good thing/bad thing

47 **Opioids and Behavior Medications**

- Fentanyl patches minimize 1st pass metabolism
- Methadone highest Q-T prolongation capacity
- Oxycodone dose dependent Q-T prolongation
 - Amitriptyline prolongs Q-T in K9

- Morphine cardioprotective rats, lowest fibrillation rate humans
 - Histamine release ☹
- Hydromorphone: no QT prolongation
- Tramadol is a serotonin reuptake inhibitor
 -

48 49 **Medications for Later**

- Long lasting
 - Parent compound and/or metabolites alter receptors
 - Take 2-6 weeks to take effect
 - Low risk for disinhibition, sedation ($\neq 0$)
 - All metabolized by the liver
- SSRIs
TCAs
Azapirone
MAOI

50 **Selective Serotonin Reuptake Inhibitors**

- Side effects most common 1st two weeks
- 4-6 weeks to see anxiolytic effects
 - down regulation of an inhibitory auto-receptor
- Fluoxetine
 - Most likely to cause sedation, inappetance
- Sertraline
 - 90% Enteric clearance, least sedating
- Paroxetine
 - Mildly appetite increase, anti-cholinergic

51 **Fluoxetine/Reconcile™ (Prozac)**

- 0.5-1.5 mg/kg Q24
- Reconcile™ flavored chew (8/16/32/ 64mg)
- Reduced serum 5HT (more in synapse? Change in turn over?)
- Hepatic metabolism, renal clearance
- Side effects: sedation, inappetence w/ weight loss, change in platelet function, *idiopathic urine retention*

52 **Fluoxetine/Reconcile(Prozac)**

- @ 8 weeks 90% reduction in urine spraying rate (Pryor, 2001)
- More effective than clomipramine for spraying (Hart, 2005)
- 10% bioavailable transdermally in cats (Ciribassi 2003)
- Successfully used to treat hyperesthesia syndrome with trauma to the tail in 1 cat (Batle et al 2019)
- Case reports in inter cat aggression (Bennett, 2018) and case series using it for compulsive behavior (Overall, 2002)
- Commonly prescribed for elimination behaviors, anxieties, aggression, compulsive disorders (Kaur 2016)

53 **Sertraline/ Zoloft**

- 0.5-1.5mg/kg
- No FDA label for animals

- No placebo-controlled trials
 - Case series use for psychogenic alopecia in cats- 1/11 cats (Saywer 1999)
 -
- 54 **Paroxetine / Paxil**
- 0.5-1mg/kg Q24 Fel
 - No FDA label for animals
 - No placebo controlled trials
 - Case report for urine marking and intercat aggression (Pryor 2003)
 - Highest risk of urine retention of SSRIs
 -
 -
- 55 **Tricyclic Anti Depressants**
- Inhibit reuptake of 5HT, NE, DA
 - Twice daily
 - 3-5 weeks to see anti-anxiety effects
 - Pro-arrhythmogenic
 - Anti-cholinergic
 - Anti-histaminergic
- 56 **Tricyclic Anti Depressants**
- Clomicalm™ (Clomipramine)
 - Pork liver flavored*
 - \$\$\$\$
 - Amitriptyline
 - No label
 - Less serotonergic
 - More anti-histaminic
- 57 **Clomicalm™ (Clomipramine)**
- 0.5-1.5mg/gk Q24
 - Feline Urine Marking (Landsberg 2005, Hart, 2005)
 - Feline compulsive disorder (Seskel 1998; Overall 2002)
 - Psychogenic alopecia (Mertens 2006)
 - Anxiety related disorders (Lister, 2000)
- 58 **Azapirone (Buspirone/ Buspar)**
- 0.5-1mg/kg Q12 Feline
 - serotonin agonist, non-sedating
 - Transdermal bioavailability below level of detection
 - Side effects increased aggression
 - rarely GI upset
 - “Bravery Drug”
 - Social bonding
- 59 **Azapirone (Buspirone/ Buspar)**
- Not useful for psychogenic alopecia (Sawyer, 1999)
 - 55% of cats had >75% reduction in urine spraying w/in first week (Hart, 1993)

- Not as good rates as fluoxetine, faster
- Reported to CAUSE aggression
- Often picked for a 'target' slinky cat in intercat aggression

60 **Selegiline (Anipryl)**

- 0.5-1mg/kg Q24
- FDA approved to slow progression Canine Cognitive Dysfunction
- MAOI: Monoamine Oxidase Inhibitor
 - Prevents metabolism of DA
 - Decreases free radicals (tangles, neuronal death?)
 - Decreases lipofuscin accumulation

61 **Selegiline (Anipryl)**

- Hepatic metabolism, renal clearance
 - No active metabolites
 - In dogs inconsequential levels of amphetamine, cats?
 - Weakly inhibits CYP3A4
- Side effects: GI upset, diminished hearing, aggression
- Interactions: ANY serotonergic medication
 - Need 2 weeks Selegiline → SSRI (5 weeks Flu →Selegiline)
 - Sympathomimetics, sympatholytics, prednisone, metronidazole, TMS, opioids (other than oxymorphone and torb)

62 **Meds for Later Example**

- 3 year old FS DSH
- FRAPs 6-8x/daily, unable to keep healthy weight
- CBC/Chem/T4 wnl

63 **For patients on daily medications**

- Trazodone
 - May increase risk of serotonin syndrome
 - Concurrent serotonergic medications may be contraindicated
 - Cerenia, tramadol, mirtazapine
- TCAs
 - May decrease blood pressure effects of clonidine and increase sedation

64 **Meds for Later Example**

- 3 year old MN
- Tries to crawl into o's clothes for fireworks, has FIC associated with loud noises
- Expecting a baby in 6 months
- Struggles to settle 24/7, has knocked over furniture near self during FRAPs, outdoor access helps a little
- Aggression out of arousal at anything near (incl ppl)
- Med Choice: clomicalm

65 **Meds for Later Example**

- 3 year old MN
- Tries to crawl into o's clothes for fireworks, has FIC associated with loud noises
- Expecting a baby in 6 months
- Building an expansion for nursery- starts next week
- Med Choice for now: Gabapetin/lorazepam
- Med for later: reconcil

66 **Polypharmacy no-nos**

- Selegiline and
 - SSRI/ TCA
 - Trazodone
 - Tramadol
 - Clonidine
 - Acepromazine
- TCA, SSRI, trazodone and tramadol
- Sileo and Clonidine
- Sileo/clonidine and acepromazine
- SSRI and TCA*

67 Polypharmacy

- Multiple NTs is how the brain regulates systems
- Doesn't mean you HAVE to be comfortable with it
- Start a 'now med' and refer

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