Anxiety

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Anxiety disorders

- Symptoms and disorders common in community settings, primary and secondary care
- Considerable personal and societal burden
- Diagnosis missed, inadequate treatment
- Range of anxiety disorders
- Co-morbidity with other psych. disorders (especially depression – 33%)
- Complete recovery is rare

Anxiety Disorders

1. Generalised Anxiety Disorder (GAD)
2. Panic Disorder (PD)
3. Social phobia (social anxiety disorder)
4. Post traumatic stress disorder (PTSD)
5. Obsessive-compulsive disorder (OCD)

Management of anxiety

1. Accurate diagnosis
2. Acute treatment (12 weeks)
3. Continuation treatment (6 months)
4. Relapse prevention
5. Approaches for patients who do not respond to first-line treatments (treatment resistance)

Pharmacological treatments general issues

1. Discuss benefits and risks of specific drug treatments with patients before treatment
2. SSRIs are effective across the range of anxiety disorders; generally suitable first-line treatment
3. Benzodiazepines effective in many disorders; short term use only
4. Other drugs (TCA, MAOI, antipsychotics, anticonvulsants) may occasionally be appropriate
5. Possible early adverse effects and worsening of symptoms (and emergence of suicidal ideation)
6. Monitor for discontinuation symptoms, rebound anxiety and withdrawal / dependence on stopping the drug

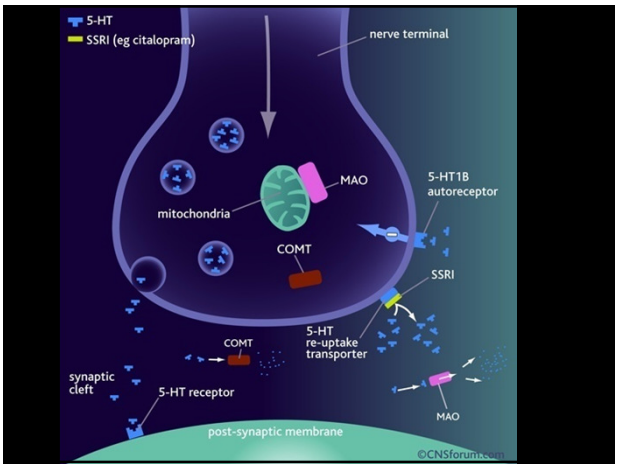
SSRIs and Venlafaxine

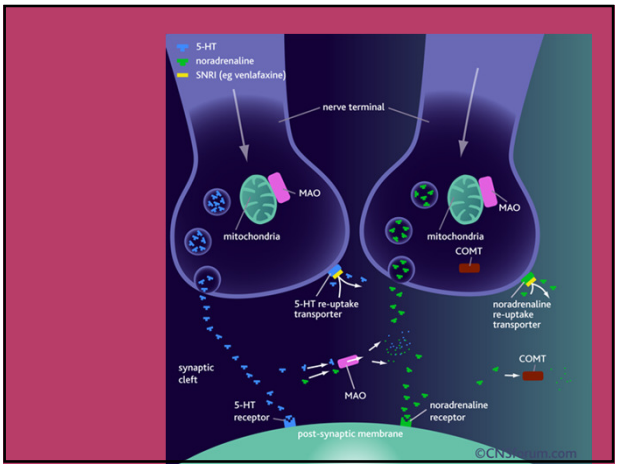
- Broad spectrum of anxiolytic effects
- Generally well tolerated
- Potential troublesome effects:
  - Initial increased nervousness
  - Insomnia
  - Nausea
  - Sexual dysfunction
- abrupt cessation (discontinuation syndrome):
  - Dizziness
  - Insomnia
  - Flu-like symptoms
- Venlafaxine should be instituted by specialist with cardiac monitoring (ECG, BP, electrolytes)

SSRIs

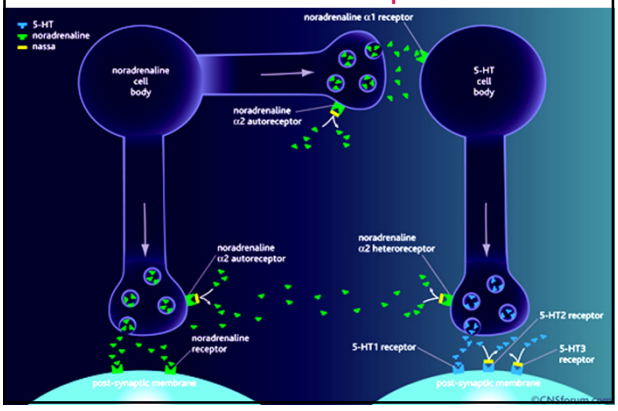
- Escitalopram
- Paroxetine
- Fluoxetine
- Fluvoxamine
- Paroxetine
- Sertraline

Proven benefit for acute (12 weeks) and long term (6 months) treatment of anxiety disorders





NaSSA: Mirtazapine



TCAs and MAOIs

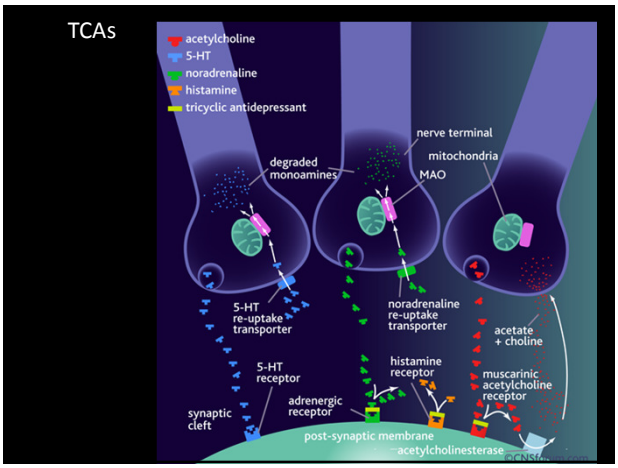
TCAs
- Greater burden of adverse effects
- Therefore, for non-response or poor tolerance of SSRIs / SNRIs in some anxiety disorders
- Avoid in suicide risk (CNS, cardiac toxicity)

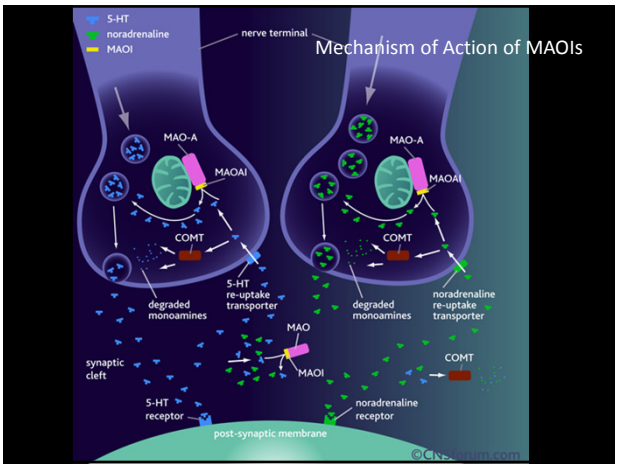
MAOIs (phenelzine - irreversible)
- Proven efficacy in panic disorder and social phobia
- Need to follow dietary restrictions

MAOI (moclobemide –reversible)
- Efficacy in panic disorder and social phobia

TCAs in Anxiety disorders

Most widely used and recommended:
- Clomipramine
- Imipramine





Benzodiazepines

- Some have proven efficacy in:
  - Panic disorder
  - GAD
  - Social phobia
- Troublesome effects
  - Sedation in acute treatment
  - Dependence with longer term use
  - Discontinuation symptoms peak at 2 days (short acting) and at 4-7 days (long half-life)
- Reserved for patients who have not responded to at least 2 treatments

Benzodiazepines in Anxiety disorders

- Alprazolam
- Lorazepam
- Clonazepam
- Diazepam

- Should be avoided if at all possible for treating anxiety
- If used, no longer than 2-4 weeks max.
- Flumazenil is a short acting benzodiazepine antagonist

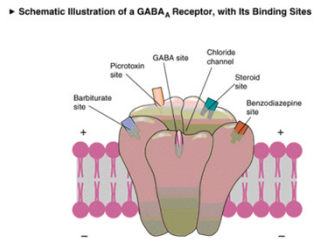
Benzodiazepines

- Anxiolytic (iv midazolam: anterograde amnesia)
- Anticonvulsant (clonazepam)
- Muscle relaxants (in neurological disease, acute dystonias)
- Hypnotics (short term management of insomnia)

Mechanism of action Benzodiazepines

- Bind to GABA receptor chloride channel complex
- Facilitate opening of channel in presence of GABA
- Increasing hyperpolarisation-induced neuronal inhibition

GABA receptor



Benzodiazepine CNS Adverse Effects

- Sedation
- Memory disturbances
- Cerebellar: ataxia, dysarthria, motor inco-ordination,
- Blurred vision, diplopia
- Vertigo
- Confusion
- Apathy
- Outbreaks of rage and violence

Benzodiazepines Other adverse effects

- Stimulation instead of sedation
- Anti-social behaviour
- Hallucinations during induction of sleep
- Depression / suicide
- In pts with organic brain disease: tremulousness, crying episodes, [impaired], agitation, confusion
- Inhibition of slow wave (stage 4) sleep
- Uncommon allergic reactions

Intravenous diazepam adverse effects

- Cardiovascular and respiratory depression
- Local pain and phlebitis

Benzodiazepines drug dependence and withdrawal syndrome

Large doses for prolonged periods

- Perceptual distortions
- Visual and auditory hallucinations
- Paranoia
- Depersonalisation
- Paraesthesia
- Perspiration
- Headaches
- Blurred vision
- Dyspepsia
- Influenza-like symptoms

Benzodiazepines pharmacokinetics

- Well absorbed orally
- Erratic absorption via intramuscular route, (except lorazepam: reliable + rapid)
- Highly protein bound
- Entero-hepatic recirculation (second round of sedation!)
- Metabolised in liver with active metabolites prolonging the half life
- Single daily dose sufficient

Benzodiazepines drug interactions

- Acute potentiation of sedative effects of:
  - Alcohol
  - Antihistamines
  - TCAs
- Cimetidine inhibits benzo metabolism
- Omeprazole inhibits diazepam metabolism
- Erythromycin inhibits midazolam metabolism
- Older anticonvulsants induce metabolism of clonazepam

Other agents...

Non –benzodiazepine anticonvulsant drugs: (Pregabalin, gabapentin, tiagabine)

- Proven efficacy in GAD and social phobia
- Reserved for third / fourth line use

Antipsychotic drugs: (trifluoperazine, Haloperidol, Quetiepine)

- Mainly for OCD as third / fourth line Rx

Remember psychological Rx :CBT, exposure Rx, cognitive Rx by trained and supervised staff

And self-help groups

Special considerations

Children / adolescents:
- Only for those who have NOT responded to psychological Rx and where benefits outweigh the risks
- SSRIs, NOT benzos, TCA's

Elderly:
- Consider comorbidity, drug interactions, lower doses, increase sensitivity to effects

Cardiac disease, epilepsy:
- Avoid TCAs and Venlafaxine

Pregnancy and breast feeding:
- Avoid drugs if possible
- Fluoxetine or TCA

Referral to specialist
- Usually an option!

Acute Anxiety (the 'B drugs')

- **B**enzodiazepines
- **B**usprirone
  - 5-HT1 receptor agonist
  - 5mg po tds
  - Low dependence and abuse potential
  - Response to treatment may take up to 2 weeks
  - But licensed for short term use only
  - Adverse effects: nausea, dizziness, headache, nervousness, excitement
  - (clinicians remain unconvinced about its efficacy)

Hypnotics (the 'Z drugs') for short term insomnia (2 weeks max)

- Tolerance to their effects occurs within 3-14 days of continuous use
- Avoid in children and elderly if possible
- Benzodiazepines: loprazolam, temazepam, triazolam
- Benzodiazepine receptor agonists (BZRA):
  - Zolpidem (short acting)
  - Zopiclone (short acting)
  - Zaleplon (v. short acting)

	Chronic Anxiety disorder	Acute anxiety	Acute Insomnia
	Social phobia, panic disorder, GAD, PTSD, OCD		
1st line	**S**SRI **S**NRI	**B**enzodiazepine **B**uspirone	Benzodia**z**epine **Z**olpidem **Z**opiclone
2nd line	TCA MAOI		
3rd line	Benzodiazepines (long acting)		
4th line	Anticonvulsants Antipsychotics		