

Psychopharmacology in Traumatic Brain Injury: Antidepressant Medications

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Overview of Psychotropic Medications

- **Antidepressants**

- Mood Stabilisers
- Antipsychotics
- Sedatives
- Anxiolytics



Antidepressants – Indications/Diagnosis

- Depressive Disorders
- Anxiety Disorders, including Panic Disorder
- Bipolar Disorders
- Trauma and Stress Disorders (PTSD)
- Obsessive Compulsive Disorders
- **TBI - NEUROPSYCHIATRIC & NEUROBEHAVIOURAL
DISTURBANCES**





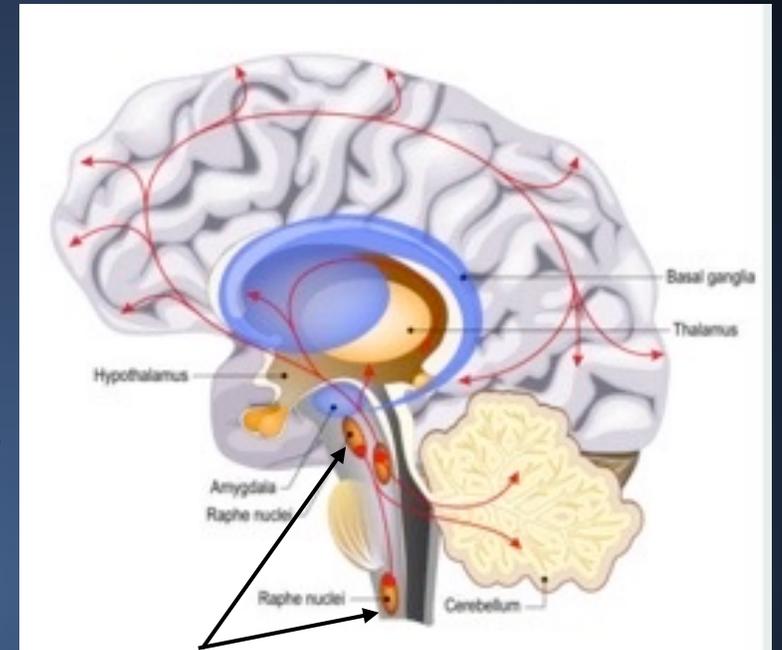
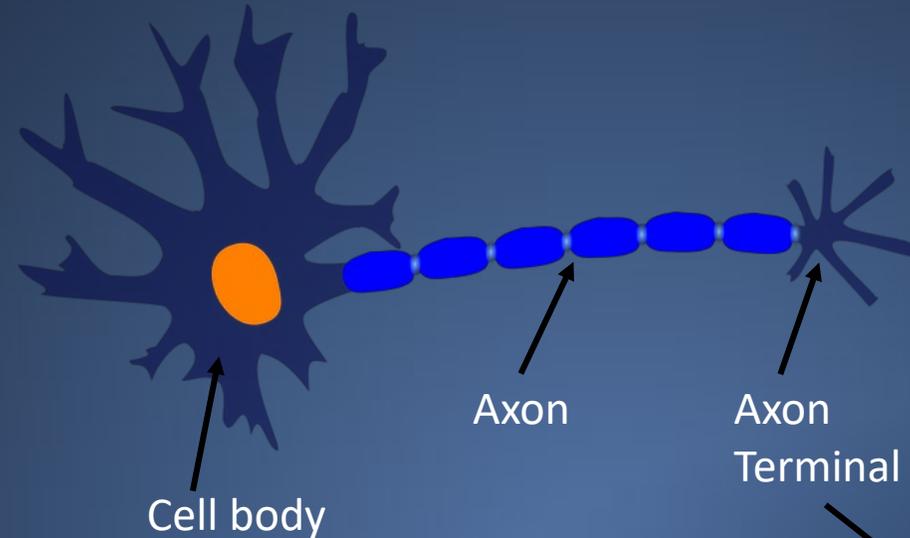
Antidepressants in TBI - Indications

- Emotional Dyscontrol
 - Pathological Laughing & Crying
 - Affective lability
 - Irritability
- Behavioural Dyscontrol
 - Agitation
 - Aggression
 - Impulsivity
- Apathy



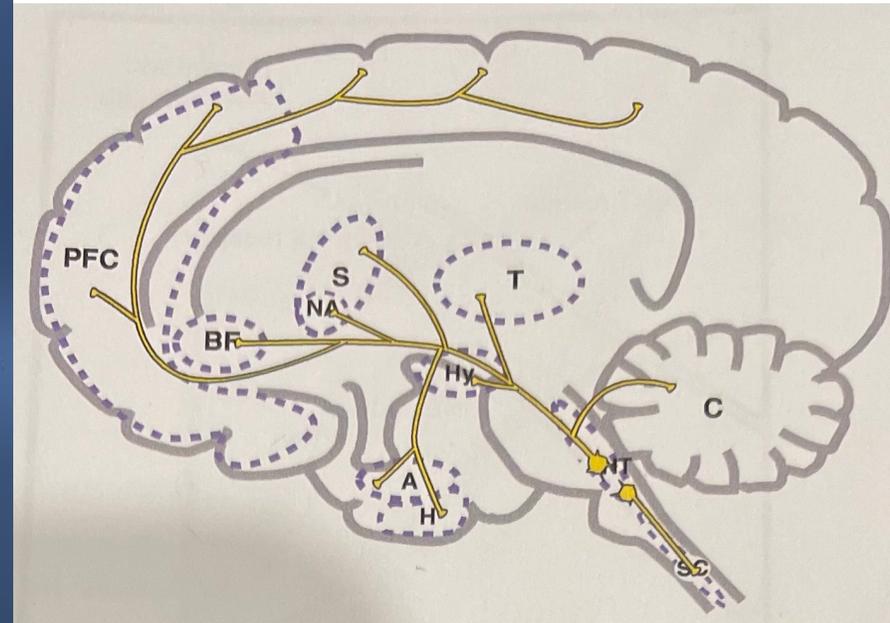
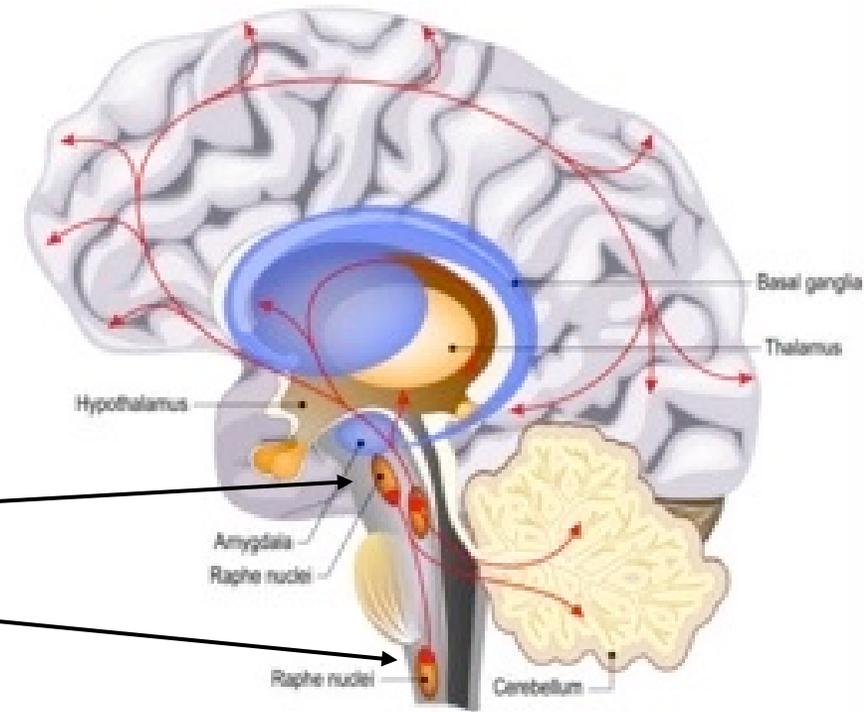
NEUROTRANSMITTERS

- **SEROTONIN**
- **NORADRENALINE**
- **DOPAMINE**
- HISTAMINE
- ACETYLCHOLINE
- GAMMA AMINOBUTYRIC ACID (GABA)
- GLUTAMATE



Serotonin

- 5-hydroxytryptamine (or 5-HT)
- Produced and released from neurons in brain stem Raphe Nuclei
- Ascending projections to multiple cortical and sub-cortical areas
- Regulates mood, arousal, cognition & sleep
- Serotonin transporter called SERT

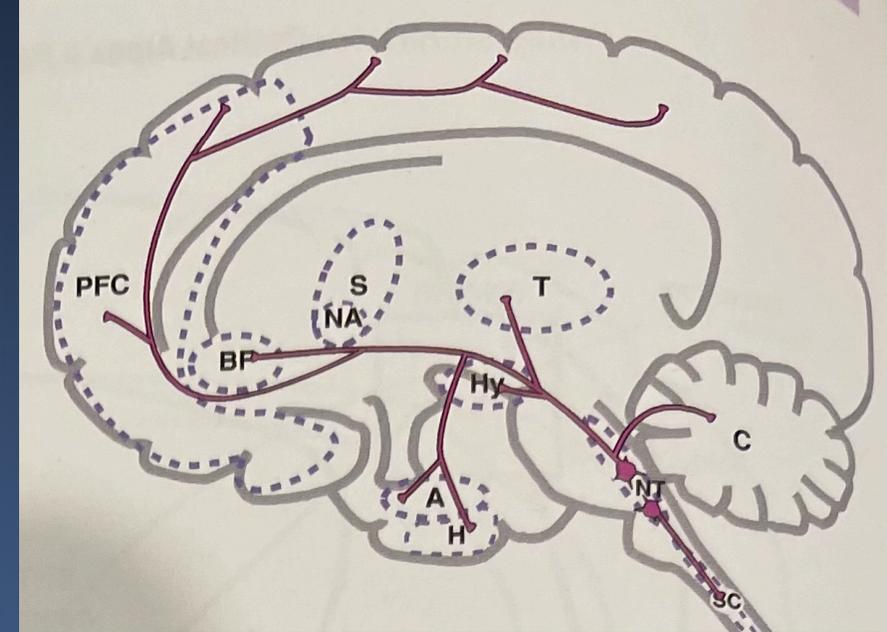


- PFC – prefrontal cortex; C – cerebellum; T – thalamus; A – amygdala; BF – basal forebrain; H – hippocampus; S – striatum; NA – nucleus accumbens; SC – spinal cord; Hy – Hypothalamus – NT – brainstem neurotransmitter centres

Noradrenaline

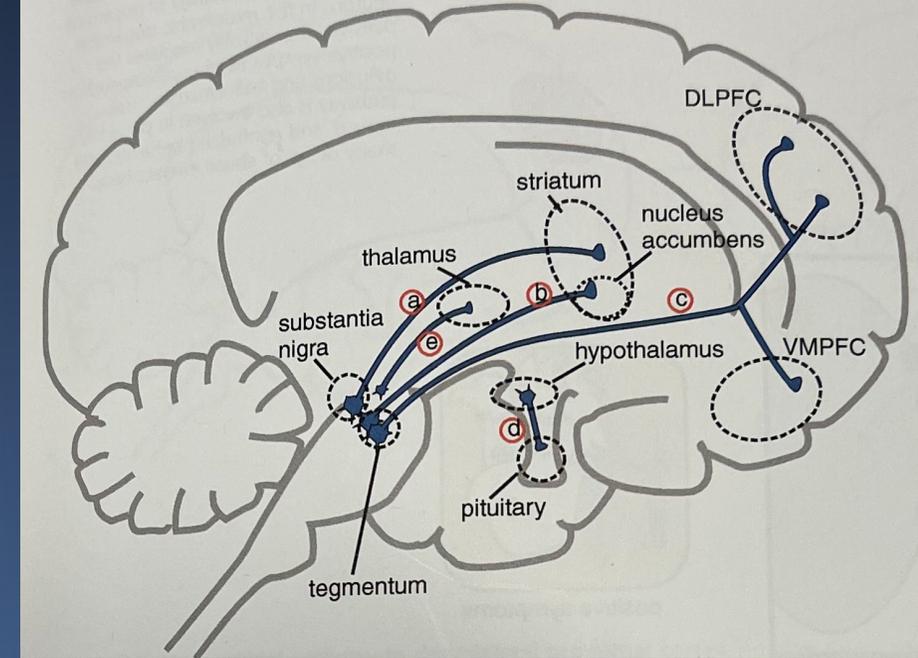
- Produced from amino acid Tyrosine
- Produced and released from neurons in brain stem Locus Coeruleus
- Ascending projections to multiple cortical and sub-cortical areas
- Regulates mood, arousal, cognition
- Noradrenaline transporter called NET

- PFC – prefrontal cortex; C – cerebellum; T – thalamus; A – amygdala; BF – basal forebrain; H – hippocampus; S – striatum; NA – nucleus accumbens; SC – spinal cord; Hy – Hypothalamus – NT – brainstem neurotransmitter centres



Dopamine

- Produced from amino acid Tyrosine
- Five key dopamine pathways in the brain
- Dopamine produced within these five different sites
- Ascending projections to multiple cortical and sub-cortical areas
- Each pathway has a different role



Antidepressant Medication Classes

- SSRIs – Selective Serotonin Reuptake Inhibitors
- SNRIs – Serotonin Noradrenaline Reuptake Inhibitors
- TCAs – Tricyclic Antidepressants
- MAOIs – Monoamine Oxidase Inhibitors
- Others – Atypical Antidepressants



SSRI – Selective Serotonin Reuptake Inhibitors

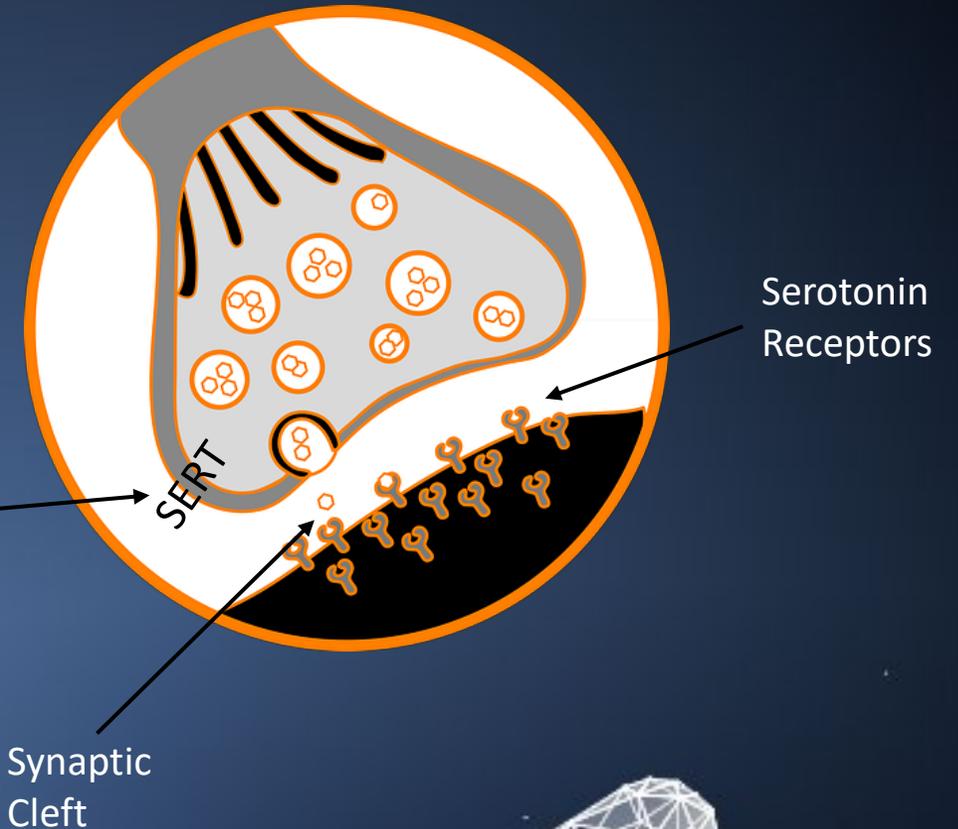


- Citalopram (Cipramil)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac/Lovan)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Sertraline (Zoloft)



SSRIs – HOW THEY WORK

- Decrease action of presynaptic serotonin reuptake pump
- Inhibits the serotonin reuptake transporter on presynaptic serotonin neuron
- Increase amount of serotonin neurotransmitter
- Increase serotonergic activity in cleft
- Sensitization of serotonin receptors
- Increase serotonergic transmission



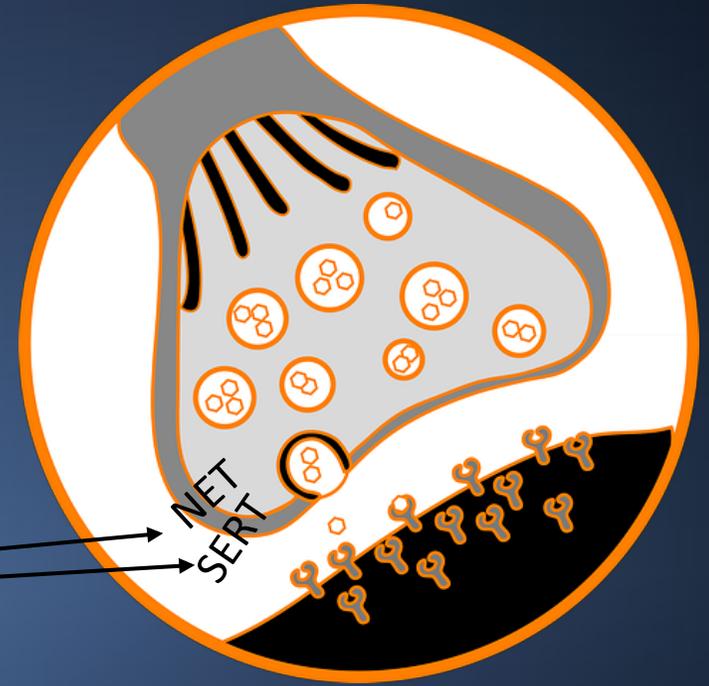
SNRI – Serotonin Noradrenaline Reuptake Inhibitors

- Venlafaxine (Effexor)
- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)



SNRIs – How They Work

- Inhibits the serotonin & noradrenaline reuptake transporter on presynaptic serotonin neuron
- Increasing the amount of serotonin & noradrenaline



SSRI, SNRI – Side Effects

Common, transient, benign:

- Abdominal discomfort +
- Nausea/Vomiting +
- Drowsiness/Sedation -/+
- Anxiety +
- Insomnia +

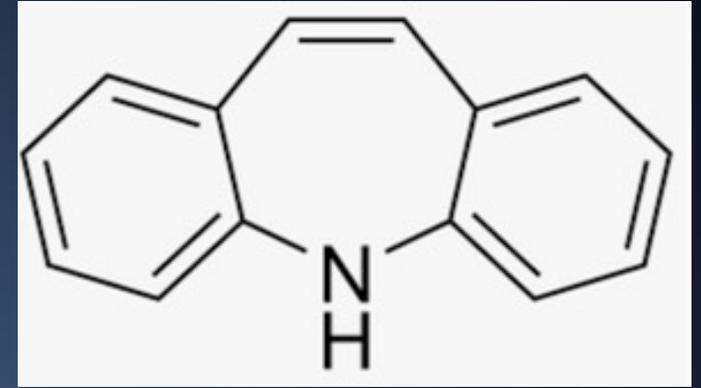
Important, rare or severe:

- Sexual dysfunction ++
- Hypertension
- Serotonin Syndrome +++
- Low blood sodium +++
- Heart Conduction defects -/+



- No side effect; + Mild; ++ Moderate; +++ Severe

TCA – Tricyclic Antidepressants

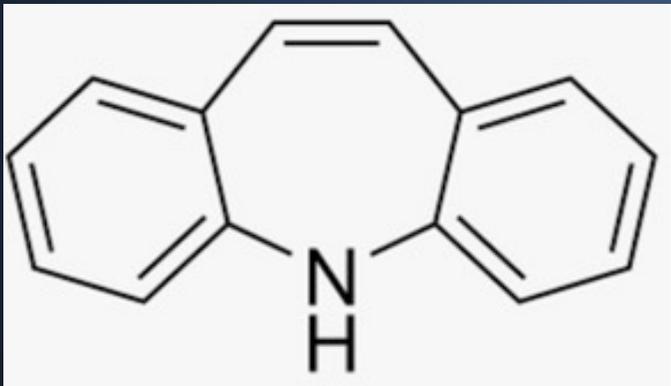
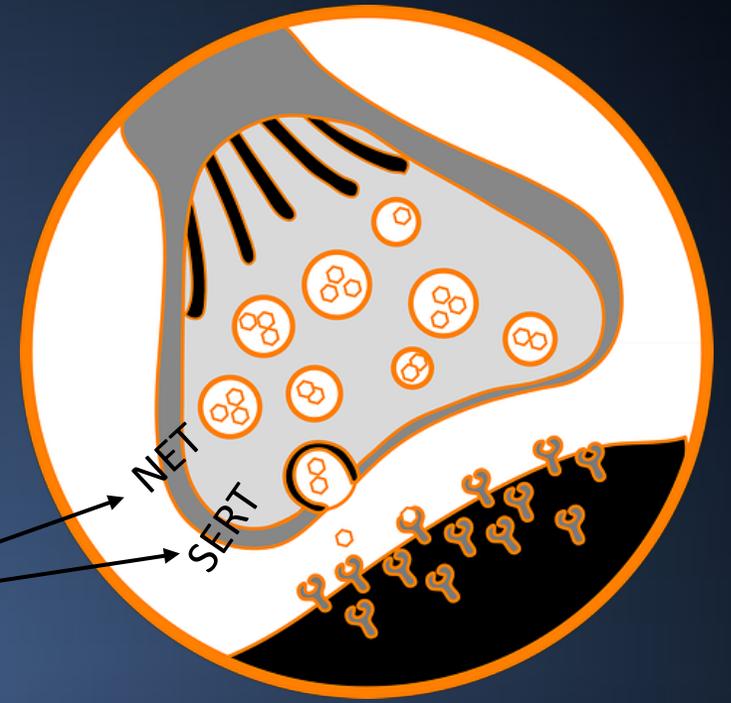


- Nortriptyline (Allegron)
- Amitriptyline (Endep)
- Clomipramine (Anafranil/Placil)
- Doxepin (Deptran/Sinequan)
- Desipramine
- Imipramine



TCA – How They Work

- Tri – 3 ring chemical structure
- Initially produced as antipsychotics
- Block Noradrenaline & Serotonin reuptake
- Very effective antidepressant agents.
- Histamine, Acetylcholine & Alpha-adrenergic receptors



TCA – Side Effects

Common:

- Drowsiness/Sedation+++
- Weight gain ++
- Low blood pressure+++
- Dizziness +++
- Nausea/Vomiting+

Common:

- Constipation++
- Urinary retention++
- Blurred vision++

Rare, severe:

- Sexual dysfunction+ / +++
- Serotonin Syndrome
- Heart defects+++



- No side effect; + Mild; ++ Moderate; +++ Severe

MAOI – Monoamine Oxidase Inhibitors

- Moclobemide (MAO-A)
- Tranylcypromine (Non-selective)
- Phenelzine (Non-selective)
- Selegiline (MAO-B)



MAOIs – How They Work

- Inhibit monoamine oxidase
- Enzyme in the brain
- MAO-A & MAO-B
- MAO-A metabolises serotonin, noradrenaline, dopamine, tyramine
- MAO-B metabolises dopamine, tyramine



MAOI - Side Effects

Common, transient, mild:

- Drowsiness/sedation +
- Hypotension +/-
- Urinary retention +/-
- Visual disturbance +/-
- Constipation +/-

Rare, but severe:

- Sexual dysfunction +
- Serotonin Syndrome
- Heart conduction defects +
- HYPERTENSIVE CRISIS +++

- No side effect; + Mild; ++ Moderate; +++ Severe



Others – Atypical Antidepressants

- Reboxetine – NRI (Noradrenaline Reuptake Inhibitor)
- Vortioxetine – Serotonin Modulator
- Trazodone – Serotonin Modulator
- Mirtazapine – NaSSA (Noradrenergic and Specific Serotonergic Antidepressant)
- Agomelatine – Melatonin agonist; Noradrenergic/Dopaminergic antidepressant
- Bupropion – Noradrenaline/Dopamine reuptake inhibitor (Nicotine antagonist)



Prescribing Principles

- Patient education (& others)
- They don't work if you don't take them!
- They are regular medications, not PRNs
- Start Low, Go Slow (but go)
- An injured brain is a vulnerable brain
- One thing (medication/treatment) at a time
- Continuously reassess clinical condition



Be aware of....

- Medication withdrawal symptoms if ceased abruptly
- Red flag side effects – Serotonin Syndrome
- Alcohol and substance use
- Additional medications
- Alternative ‘natural’ medications
- Worsening symptoms



What we have covered

- Antidepressant medications
- What we use these medications for
- Neurotransmitters involved
- Classes of antidepressant medications
- How they work
- Side effects
- Prescribing principles



Questions?



Disclaimer

The information provided in the presentation is of a general nature. Any decisions regarding treatment for individual patients should always be made in consultation with the patient's medical practitioner.



References

- Textbook of Traumatic Brain Injury. 3rd Edition. Silver, McAllister, Arciniegas.
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