effect of some of the cognitive treatments is that they exacerbate problems with the dopamine system.

Anti-depressants

The main disorders of mood are major depressive disorder & bipolar disorder:

- Major depressive disorder (MDD) is characterised by more than 2 weeks depressed mood, pessimism/melancholy, loss of enthusiasm for activity and loss of confidence, feelings of guilt, trouble concentrating, changes to sleep (e.g. insomnia or early morning awakening), and appetite changes plus some other minor symptoms. There are no manic episodes in MDD but suicidal thoughts and attempts are common. MDD is commonly accompanied by anxiety and phobias, which are also treated by MDD specific treatments.

- Bipolar disorder (BD) is characterised by mood swings between mania (>1 week) and depression, which is typically a longer and more frequent phase. During the manic phase the patient will typically be euphoric, irritable, energetic with very little need to sleep, impulsive, and excessively engaged with pleasurable activities of goal-directed activities but with poor judgement e.g. they'll believe they have the secret to the stock market and put all their money on that hunch. The treatment for BD is different to MDD because it focuses more on mood stabilisation - keeping the patient not too low and not too high. BD is an interesting disorder because many sufferers say that they wouldn't cure the disease if they could. They simply find the manic phases too enjoyable to give up.

Treatments

There are several avenues of treatment for MDD and BD. The most well-known treatment is drugs but there is also cognitive based therapy (CBT), and electroconvulsive therapy (ECT). Cognitive based therapy is a psychotherapy (patient talks to psychologist) used to change the patient's patterns of thought, feeling, and behaviour by giving them practical self-help strategies - they train you how to cope. ECT is a last resort therapy for mood disorders. It is quite effective and is believed to work by similar mechanisms to the drugs. It does come with side effects namely memory loss. The drugs typically take 1-3 weeks for effects to become noticeable and 6-8 weeks for optimum efficacy. This is due to their mechanism (explained later) and is not completely understood.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) were accidentally discovered when pharmacologists were creating promethazine, a sedating anti-histamine (they also discovered some antipsychotics at the same time). The TCAs differ from the sedating anti-histamines because they have buckled rings (3) rather than flat. One of the most popular TCAs is amitriptyline. They were the first discovered anti-depressants but they have a lot of side effects so, despite their efficacy (similar to modern anti-depressants), only a few are still used. They're often used nowadays for peripheral nerve pain such as trigeminal neuralgia (face pain). The mechanisms of TCAs are:

- They are very potent inhibitors of the uptake of noradrenaline, and they also inhibit the uptake of serotonin.
- They're antagonists at α1 adrenoceptors, histamine receptors, muscarinic receptors, and serotonin receptors (in high doses). These actions are what lead to the side effects of TCAs:
  - Anti-cholinergic side effects e.g. dry mouth, constipation, urinary retention, blurred vision etc.
  - Cardiovascular side effects are believed to stem from their effects on α1 adrenoceptors and muscarinic receptors. They typically cause arrhythmias and changes in the ECG of the heart and this can be fatal, especially when combined with alcohol. They also can result in postural hypotension i.e. users may faint or fall when they get up because of insufficient sympathetic nervous system response to blood pressure changes.
  - The main central nervous system side effect is excessive sedation
  - Weight gain can occur

2nd Generation Anti-depressants

The 2nd generation anti-depressants are a group of anti-depressants developed in the ~1970s without the extensive side effects of TCAs. The most popular group of 2nd generation antidepressants is the selective serotonin reuptake inhibitors (SSRIs), which have low toxicity & work by inhibiting the reuptake of serotonin specifically. Fluoxetine (trade name Prozac) is the most well-known SSRI. The main side effects of SSRIs are:

- Insomnia, sexual dysfunction, gastrointestinal disturbances, restlessness, anxiety (early in use), and recently some people have been claiming that they increase suicidal thoughts although there's not a huge amount of evidence for this.

Some other 2nd generation antidepressants include (don't need to memorise):

- Venlafaxine is an inhibitor of both serotonin and noradrenaline reuptake, and also a weak inhibitor of dopamine reuptake.
- Mirtazapine is an antagonist at α2 adrenoceptors, and 5-HT2 and 5-HT3 receptors. It helps depression mainly by inhibiting α2, which increases noradrenaline levels (and noradrenaline typically increases serotonin too). It can cause weight gain.
- Reboxetine is an inhibitor of noradrenaline reuptake, & a weak serotonin reuptake inhibitor.

Monoamine Oxidase Inhibitors

The monoamine oxidase inhibitors (MAOIs) were discovered in the 50s by accident. The hydrazine and non-hydrazine varieties have considerable side effects due to the cheese effect (tyramine containing foods cause hypertensive crises because MAO in the gut is inhibited and can't break tyramine down - noradrenaline is displaced onto the synapse by tyramine) so they're not used anymore. Moclobemide is a reversible inhibitor of monoamine oxidase A that is the only MAOI still used because the cheese effect is minimal. It's not widely used but it can be quite

efficacious for mild depression. The other typical side effects include dizziness, insomnia, and nausea.

Treatments for Bipolar Disorder

The main mood stabilising treatment for BD is lithium carbonate, which has a narrow therapeutic range (doubling the therapeutic dose can be toxic - blood levels must be measured regularly) but is quite efficacious. The main side effects of lithium are:

- Renal problems caused by lithium replacing sodium. People with existing renal problems can't take lithium.
- Lithium inhibits the thyroid, which causes the thyroid to enlarge.
- There are a number of neurological side effects at higher doses of lithium: shakes, convulsions, coma, death etc.

Not much is known about how lithium works. It is believed that it interacts with 2nd messenger systems, principally the PIP2 signaling cascade, and affects levels of other neurotransmitters.

Anti epileptic drugs (e.g. valproate, carbamazepine) and antipsychotic drugs (e.g. chlorpromazine, risperidone) may also be used. The anti-epileptic drugs also act as mood stabilisers but the antipsychotics will typically be used for other symptoms more relevant to antipsychotic and sedative actions.

Mechanisms

Until recently it was thought that TCAs, MAOIs and SSRIs are effective for depression because they increase monoamine (noradrenaline, serotonin, dopamine) levels - monoamine theory of depression. However, recent studies have shown that this is not necessarily true, especially since the drugs take weeks to work despite changes the neurotransmitter levels instantly. These studies suggest that desensitisation of β-adrenoceptors, 5-HT2 receptors, and α2 adrenoceptors may be more important than altered neurotransmitter levels. Another recent area of interest is the role that increased cortisol might play in depression, and decreased brain-derived neurotrophic factor (or malfunction of its receptor TrkB). Neuronal loss in the prefrontal cortex and hippocampus may be involved too. Many antidepressant therapies reverse this loss by stimulating neurogenesis.

Pain Control

Pain is described by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". It's a vital defensive mechanism however if it's uncontrolled it can become a disease in itself. Chronic pain syndromes (pain for >3 months) are debilitating and also lead to indirect symptoms such as insomnia, depression, anxiety, anorexia, and even changes in autonomic function (cardio, bladder etc.). 1 in 5 Australia's are affected by chronic pain and a quarter of these people will have their life significantly impacted by the pain. There are 3 broad groups of chronic pain: