Topic 12: Mental Health

- The body is a chemical based machine
- Problems arise when organs work incorrectly
    - Problems can be physical
    - Problems can be chemical
- The brain is an organ
    - Problems with the brain will manifest differently than with other organs
    - It will affect our behaviour
- We can control our behaviour
    - And we assume others also have their behaviour under control
    - And when they act differently we assume it is by choice
    - However it could be due to mental health issues
    - This is what causes the Stigma around mental health
- Genetic basis for personality
    - There is also a genetic component to mental illness
        - Does not mean you will get it 100% but does contribute
- Once thought to be caused by demons
    - Trepanation
        - Cut a hole in head to allow brain to 'breathe'
        - Sometimes would alter brain
- Mentally ill were tortured
    - This is because we thought behaviour was under our control
    - So it was a punishment
- In history mentally ill were placed in asylums and prisons
- Freud developed psychotherapy in 1896
    - First change in attitude towards mental illness
    - Tried to actually treat the problem
- Lobotomy:
    - Insert needle through eye sock and wiggle it around the brain
    - Separates one lobe from another
    - Tends to have a calming effect on people's behaviour
    - Stopped practicing in the 50s/60s
        - Realized they weren't actually helping the person with the condition
- Electroshock therapy
    - Will give a remission for certain conditions
    - In the 50s they would strap you down and put a piece of rubber between your teeth and shock you
        - Extremely painful & traumatic
    - Still practiced today
        - We sedate them when they get shocked
    - Not used for everything
    - Can be effective but we are not sure why
- In North America treatment started to change in the 1950s
    - They were treated in a medical way
    - Asylums were converted to mental hospitals

- In the 1950s were discovered the first effective drugs for mental problems
- Schizophrenia
    - Loss of contact with reality
    - Person slowly progresses into and alternate reality
        - Auditory hallucinations
        - Confused thinking
        - Magical thinking
            - Your thoughts have an effect on the world
        - False beliefs
        - Anxiety disorders
        - Feelings of persecution
        - Lack emotion
    - Antihistamines were used to calm surgical patients
        - Was used to alleviate the anxiety of people with schizophrenia
        - By accident it also helped with their other symptoms
        - In 25% of cases people were able to leave the hospital and function in society
            - Because there were more in touch with reality
        - Long term use side effects (similar to parkinson's)
            - Grimacing
            - Dyskinesia
            - Lip smacking
        - The fact that these drug work lead to our theory on how schizophrenia works
            - Thorazine was a dopamine antagonist
                - Reduces psychosis of schizophrenia
            - Amphetamines raise dopamine amounts in the brain
                - Produce psychosis similar to schizophrenia
            - Theories explaining schizophrenia based on drug effects
    - Dopamine Antagonism
        - There are at least 5 receptor subtypes
            - D_1 to D_5
            - Allow dopamine use in different parts of the brain
            - Create different pathways for dopamine to transfer information
                - Improves messaging
        - D_2 receptor most important
            - Early antipsychotics were all D_2 antagonists
                - Not very clean drugs:
                    - Lots of side effects
                    - Targeted too many dopamine receptors:
                        - D_2 antagonists
                        - D_1, D_3, D_4 antagonists
                        - Serotonin antagonists
                        - Adrenaline antagonists
                        - Acetylcholine antagonists

                - Histamine antagonists
        - Discovery of subsequent drugs
            - Discovered using animal testing
            - Researcher identify patterns of behaviour when the animal has no drug in the system
            - Then they administer the drug known to treat an issue to the animal and identify changes in the normal behaviour
            - They then look for new drugs that cause the saem changes to behaviour
    - Atypical Antipsychotics (1972)
        - Clozapine
        - Weak D_2 dopamine antagonist
        - Strong serotonin agonist (5-HT)
        - Less likely to cause motor-control disabilities/side effects
        - Reduces symptoms differently
- Depression
    - Unable to feel happy
    - Lonely, sad
    - Anhedonia: inability to experience pleasure
    - Tricyclic antidepressants 1951
        - Part of an experiment to find drugs to treat schizophrenia
        - Imipramine
            - Mood elevators
            - Block the reuptake of serotonin
            - Lots of side effects
                - Effect lots of thing in the brain:
                    - Inhibits serotonin reuptake
                    - Inhibits norepinephrine reuptake
                    - Dopamine antagonist
                    - Acetylcholine antagonist
                    - Histamine antagonist
        - Accidental discovery of Iprozaid
            - Tuberculosis drug
            - Antidepressant effects
            - Inhibits monoamine oxidase (MAO)
                - MAO regulates the production of serotonin
                - Iprozaid reduces the destruction of serotonin
        - Theses drugs are the basis of the theory that depression arises from low serotonin levels
        - SSRI: selective serotonin reuptake inhibitor
            - Cleaner then Iprozaid
            - Prozac was the first one
                - Side effect (very uncommon)
                    - Anxiety
                    - Sleep disturbances

        - Sexual dysfunction
        - Suicidal thoughts
            - In quality clinical trials almost no difference between placebo and Prozac
- OCD
    - Affects 2%
    - Obsessive thoughts
        - Unwanted thoughts
        - Unrealistic
            - Contamination
            - Symmetry
            - Saving
            - Perfection
    - Rituals
        - If a situation does not satisfy their obsession they feel great unease and need to perform a ritual to relieve this feeling of discomfort
    - Magical thinking
        - They get a sensation that something bad will happen if they do not perform the ritual
    - Use antidepressants to treat
        - And therefore it is believed that OCD is connected with low serotonin function
- Bipolar disorder
    - Alternate between high energy, happy levels to extreme depression
    - John Cade was researching manic depression
        - Injected urine from manics into guinea pigs
        - He thought it was the uric acid causing the death
        - To buffer this he administered Li_2CO_3
            - Found it calmed the guinea pigs
            - When administered to patients the bounces between highs and lows were less extreme
            - Found in 7 Up, when it was sold as a medication at the turn of the century
            - Narrow therapeutic window
            - Mechanism of action are not precisely known
            - However it effects the brain in many ways
    - Valproic Acid
        - Anticholinergic drug
        - Mechanism not known
        - Simple structure so not much editing can be done
    - It is hard to get patients to take their meds because the manic phase feels amazing, the drugs tone down their highs
- Anxiety
    - Common
    - Fear without reason

    - Barbiturates discovered by accident in 1864
        - Not ideal drugs
            - Addictive
            - Many negative side effects
        - Magnify the effects of GABA (neurotransmitters) in the brain
            - GABA inhibits neural function
            - Agonist of GABA reduce neural activity
    - Benzodiazepines
        - Widely sold to house wives, anxiety was very commonly diagnosed to housewives
        - Amplify the effect of GABA
            - Not direct agonists
            - Increase the sensitivity of the receptor to GABA
        - GABA move using ion channels
            - The drug causes the channels to open with less GABA present
    - Valium (Mother's little helper)
- Psychiatric drug are controversial
    - “Alter brain chemistry”
        - That is the point
        - That is how the drug treats the mental illness
        - Their brain is not working properly and the drug makes it work correctly
        - Have to be taken for a long period of time, not a one and done fix
    - “Similar to placebo”
        - In certain conditions the effectiveness of the drug is the same as the placebo (%)
        - However the percentages are not comparing the same things
            - The percentage of improvement when given a placebo is the change between no treatment and those even a placebo
            - The percentage of improvement when given the drug is the change between those given a placebo and those given the drug
    - Limited effectiveness
        - Some of our new drugs are no more effective than those in the 50s
        - However there are much fewer side effects
            - Each drug produces slightly different molecular interactions
            - Side effect profiles tell you what to look for
                - Once side effects are known, drugs can be engineered to avoid or minimize them
            - Each new drug is a little better than the older ones
            - Side effects today are much less frequent
            - Some side effects are a placebo effect:
                - If you are told that you are likely to experience these side effects you are more likely to experience them, they also tend to be self reported side effects
                    - Headache
                    - Nausea

            - Anxiety
            - Sexual dysfunction
            - Depression sleep disturbances
        - We do not completely know how the brain works, which makes it hard to create perfect drugs
        - Also the drugs are not smart enough to only impact one connection
        - Human experiment are hard to perfectly control all variables
            - We typically use mice or rats because they are small and cheap
            - However their brains are not identical to ours
            - We have to try and translate the results of the drug in rats to humans
                - See how they tested schizophrenia drugs on animals
        - It is hard to measure brain activity
        - Theories on the diseases are based on the effects of a drug
            - Observe changes induced by drugs
            - Chemically we can see prozac affecting the brain with in 20 mins, however patients do no experience relief from symptoms for 3 weeks
        - Our tools used to look at the brain could be much better
    - Side effects
        - Unpleasant
        - Frequent
        - Permanent
    - Addictive
    - To a degree all of these statements are correct
- Drugs for mental health do work
    - Efficacy rate is lower than for other diseases
    - Have been improvements
        - Side effects
    - The nature of most illnesses means they can only be managed
    - “Breakthrough” drugs require
        - Luck
        - Breakthroughs in understanding of the biochemistry of the disease