w) neurotransmitters are chemicals, they are grouped together in families, based on their chemical structure e.g amino acids, monoamines, ACh. monoamines includes serotonin(5-HT), dopamine (DA), nonadrenaline (NA). (find out more about what each individual one does)

x) neurotransmitter synthesis is the same process as baking a cake from scratch...? -- butter and sugar are the precursors (ingredients) and the act of stirring is called an enzyme. Add the eggs (another precursors) add flour (another precursor) transforming the mixture, the oven heat is another enzyme acting on the precursors. Current state of knowledge is that neurons can only produce one neurotransmitter. The synthesis involves a sequence of stages(like baking a cake, adding the precursors)

y) this is an example of banging all the ingredients together in fewer stages as there is less precursors, and only one enzyme is present, (ChAT)

z) there is a diet called tryptophan diet, that might helps regulate serotonin in depressed people. Eat more food with tryptophan - bananas and turkey are very high in naturally sources of tryptophan. Helps convert 5htp to 5ht to regulate serotonin. The 5htp capsules have a minimal affect because of the route of administration (taken orally), so there is little of the drug left after digestion.

a1)

b1) dopamine is that last precursors before it's made into noradrenaline. Parkinson's is a loss of dopamine producing neurons in the brains region for starter movement, which is kickstarted by dopamine neurons, if you lose this then you experience parkinson's disease. Dopamine can increase reward and decrease risk so behaviour can became more impulsive, as less recognition for risks. The rate limiting step can be thought of as the baking stage, it takes as long as it takes, cannot be sped up or slowed down. Dopa is more effective than tyrosine because of the rate limiting step.

c1) if your brain gets flooded with dopamine (i.e cocaine) the outside of the neuron is slowed down with dopamine, slowing down production on the inside.

d1) auto receptors can monitor this. If the auto receptor is blocked, than the auto-receptor will think there is no chemical, therefore they will produce more of this, creating a build up of the chemical. Not the same as the blocking for anti depressants or reuptake for dopamine.

e1) tryptophan experiment - gave a drink that stops making of tryptp in brain, gives an indication of how efficient the serotonin system is. People using ecstasy are more effected by the tryptophan. Can be explained as damage to the serotonin system. Can you say this is an effect of taken a drugs or could it be a difference before the drugs have been taken. ANSWER -possibly, but only if tryptophan was low to start with, to make it back to the normal state.
7) Glutamate is essential for laying down new memories

Prefrontal cortex agrees with the reward fun, glutamate sends a message back to cement that ‘I enjoy doing this’ and ‘I should do it again’ This is incentive sensitization

8) people who have this defective DRD2 gene, are more likely to abuse drugs (more prone to), to become problematic gamblers or to have more addictive behaviours that release reward in the brain. This can happen with inherited genes or mutilation.

9) so when a KO mice doesn't have a transporter for dopamine reuptake, they post synaptic receptors are being stimulated more by rewards as there is more dopamine in the synapse ready available

11) the crystal form is considered more pure, the majority of drugs bought in the form of a pill are generally still mdma, or similar

Cannabis was made illegal because people were smoking it and white people didn’t like it

13) Mixmag is a dominant dance music magazine from years ago.

This was not good a sampling method because not all ecstasy users would necessarily buy the magazine.

There is no control on when people complete online surveys, the time of day, whether they’ve had a drink or had music on.

Advertising a study on a clubbing website about illegal drug use, people are a little bit wary of doing it as they are not aware of the anonymity of studies, so generally restricts the amount of people that sign up to the study.

14) This slide gives you the information on how frequently people are using drugs and how much, to use in the COURSEWORK. It is completed by drug users world wide, about what they’re taking and how they’re taking it.

15) causes a massive release, prevents reuptake of serotonin, keeps more in synapse. The massive release causes damage to the dendrite in serotonergic neurotransmitters.

In fischer et al. the rats were given huge doses 4 times a day for 4 days straight, and this is why it was portrayed as being so damaged in the brain scans of the neuron.
Nucleus accumbens is at the start of the brain's reward pathway, the hypothalamus is the part of the brain that regulates homeostatic functions, temperature control, and appetite control. The hypothalamus tells you you feel hungry and you need to eat. High density of cb1 receptors in these two areas (reward pathway and appetite control) tell you that you want to eat high rewarding food (chocolate, crisps etc)

It is reducing obesity with the cannabinoid antagonist as it decreases the amount of cannabinoid ... it is sitting on the receptors and preventing your brain's natural cannabis from working, it reduces appetite in animals, and in humans in clinical work, as it is reducing peoples desire for high calorie. It was discovered this had a side effect for serious anxiety and depression and so was removed from pharmacy. (RIMONABANT)

33)

Lecture 8

4) over 4000 harmful compounds in tobacco

Carbon monoxide is an extremely toxic gas, does't exist until the tobacco is being burnt. It attaches itself to the haemoglobin in the red blood cells, prevents oxygen from finding its way around the body in the way it should. Primary problem is leading to cardiovascular disease

Tar (total aerosol residue) - refers to all the other compounds in the tobacco smoke

Nicotine has very little effect on respiratory disease, minimum impact on cardiovascular. Nicotine is addictive however is not particularly harmful, which is why it is used as a form of treatment in NRT.

5) smoking is effective way of taking nicotine the brain. Smoked, diffused into the bloodstream, then taking to the brain through the blood. Injecting it wouldn't get it there much quicker than that. On average 1 mg of nicotine is taken in per cig by a smoker

6) cotinine can remain in the body after days of smoking a cigarette - it doesn't have any active effects. Confirm that people haven't smoked in tests we can take a urine or saliva test and detect cotinine levels. Nicotine half life is 120 minutes. After 1 day nicotine levels are back to normal

7) Nicotine receptors resembles nicotinic acetylcholine neurotransmitter, nicotine can easily bind to these receptors. They are found sparingly throughout the CNS and ANS and the neuromuscular junction. They are ligand gated ion channels
Carbon monoxide delivery to the brain causes light headedness, which some people enjoy.

Variety of chemicals added to cigarettes to make them more addictive. More reinforcing than other forms of nicotine delivery.

17) denic smoking is associated with alleviation of urges to smoke, long term it wouldn’t work. Other sensory and tactile cues have become reinforcing in their own right. Secondary/conditioned responses because they have been associated with nicotine so many times. The repetition pairing have become to be rewarding by themselves.

18) bolus theory proposes that this surge is what is so rewarding and addictive, and maybe why NRT isn’t as effective as it is hard to replicate this surge of smoking.

21) so nicotine is having a direct significant effect on cognition on the smoker. This may also be rewarding.

The problem with all these studies is that we cannot tell where it is having a significant effect. We don’t know if the abilities are before as well. So we started to included non smokers in studies.

First cig in the morning is because nicotine levels are depleted over night, so more motivated to smoke. Larger boost, and help withdrawal.

Smoking accompanies other pleasurable activities, making the enjoying activities nicer after having a cigarette. Making that other stimulus more reinforcing - enhancing the reward.

24) rats do not respond to the nicotine self adminstration becuase of the lack of other stimuli to pair it with for reward.

Place preference, rats were more likely to spend more time in the compartment with nicotine and cocaine rather than just the cocaine one.

25) one of the trials to give them card sorting tasks for money and for without money, and test the speed of which, to measure the responsiveness of reward. There was a significant effect of abstinent smokers and recent smokers, there is a clear difference in responsiveness to reward in the tasks.

26) the cognitive enhancing effect of nicotine can strengthen the ability to inhibit automatic behaviours -- interesting because addiction can inhibit the automatic behaviour??

29) were not seeing actual differences on working memory however there may be at a neurological level.
8) repeated amounts of amphetamines can present psychotic symptoms known as amphetamine induced psychosis, clinicians find it difficult to distinguish between amphetamine Parkinsons disease due to deplete DA - antipsychotics mimick this.

9) there is just too much DA in the brains of S in the area of nucleus accumbens. Dopamine hypothesis needs to be refined. Anti psychotics drugs bind to and block dopamine receptors straight away. If it was simply the act of dopamine then it must be triggering some other longer acting change.

They are only effective for the positive symptoms and may even make the negative ones even worse. If it was simply just blocking the dopamine it would alleviate all symptoms, but it doesn’t so there is something else that needs to be found.

Amphetamine increases dopamine in the brain, and this is why it is related to drug induced psychosis because of the large levels of dopamine in the brain.

10) In S if there is reduced Glutamate from the prefrontal cortex it means glutamate can’t have its usual effect on GABA, and that means GABA can’t inhibit the dopamine neurons, and because the dopamine neurons project to nucleus accumbens this means more dopamine in the nucleus accumbens.

Result increases the DA.

11) Low levels in predisposed of glutamate because they are low there isn’t enough to activate the mesocortical DA, and because of this it results in an overall reduction in receptor activity, which means there is more DA.

Too much in one place (nucleus) too little in the other (cortex) due to glutamate.

14) wide variety of symptoms can account through the wide spread of glutamate throughout the brain - the NMDA receptors are widely distributed which fits with the clusters of symptoms throughout the brain.

Causing the glutamate function, several susceptibility genes accounts for this.

15(1) drugs that mostly act on dopamine and act on broad neurotransmitter symptoms

(2) aripriprisol
(3) different mode of action.

_______ Video
This could explain why symptoms take several weeks to improve. In conclusion, there is an initial increase of dopamine but then after a while the regulation is more controlled and then the dopamine is increased.

There may be other explanations as well.

21) Because they are also working at other receptors they are causing side effects, parkinsonian like movement disorder as it working outside of the voluntary pyromidal functioning. These side effects are explained by antagonist effects at DA 5-htr, na, ach and histamine receptors.

22) Parkinsons is due to loss of DA producing neurons (tremor, slowness of movement and difficulty of initiating movement) we know that PD when there is a loss of dopamine in the brain of substantia nigra to the striatum which is called the nigrostriatal tract. Massive reduction of dopamine function in PD in this area.

When we give people with S a d2 antagonist, it has actions on dopamine receptors throughout others tracts, and thats why it creates the symptoms as it is effecting the nigrostriatal tract as well.

Increase in acetylcholine, contributes to the PD symptoms, anticholinergic drug can be given alongside the medication to help with the PD symptoms.

Blockade of dopamine is happening else where ultimately causing all this.

23) more years of use have more tardive dyskinesia (TD) symptoms, elderly patients are more vulnerable to this. Even after the drug there is resistance to the improvement of TD, unsure of what causes it.

Glutamate interacts with the mesolimbic tract, and mesocortical tract.

25) seem to be more effective at reducing cognitive and negative symptoms. Side effect profile, the biggest difference is that they have few motor side affects, (extra pyramidal or PD side effects) less parkinsons like effects.

They act more selectively on the d2, d2 is still found around the brain so it still has effects on hormonal function and motor.

Clozapine was then developed and used in the early 1990s, also an antagonist on 5-htr receptors. There was a link between LSD and the development of positive symptoms. LSD