



## **Meeting the demands of a hedonistic society**

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Good evening ladies and gentlemen and welcome to Allen & Overy. For those of you who don't know me, I used to be Gresham Professor of Physic but I am now a neuroscientist at the Babraham Institute in Cambridge. The title of my talk, which is deliberately supposed to challenge you, is 'Meeting the Demands of a Hedonistic Society,' and yes, I could have called it 'Sex, Drugs and Rock 'n' Roll', but quite a number of other people have actually used that title before me and I am trying to be a little bit more serious here!

The father of hedonism, pleasure-seeking if you like, is Aristippus, who lived around 435-346 BC, but I am not going to say anything about him, other than to point out that hedonism has been around for an awful long time.

For this lecture, the issue is whether biomedical science actually help in any way to our hedonistic ends? I am sure you read every day, both in the media and from also my colleagues, that there are magic bullets just around the corner which will sort out everything - whether you are depressed or anxious, you just want to be happy, if you want to be thin instead of fat, and so forth. But is it really true? Would in fact we be better off reducing our expectations and relying more upon lifestyle changes?

I am not going to concentrate too much on lifestyle changes here. I am going to really tell you what there is out there, and what there is likely to be out there in terms of drugs, and what is likely to be developed in the next few decades. So, in the end, you can answer the question: Is it really going to be a 'drug me happy' or must we continue to do it the hard way?

I am going to start off with a bit of neuroscience, because really this is the root of the problem. The brain has very simple and highly conserved pleasure circuits. They start off very deep in the brain. We can find these same structures in reptiles, and in highly conservative evolutions. They tend to use a neurotransmitter called dopamine, which is often called the reward transmitter, although it is involved in many other functions, including locomotion, but at these particular areas - the ventral tegmental area and its projections to the nucleus accumbens - are the basic pleasure centres of the brain. They make you feel good, and that is where pretty much all drugs that we use act as well - that's why they make you feel good.

They are also controlled in a part of the brain called the frontal cortex, which is very much evolved in primate evolution - it has become much larger. This is actually a very important part of the circuit, as far as experience of pleasure is concerned, but perhaps more important than that, it is a very important control mechanism. It is what keeps things in check. That is where your moral conscience is controlled and it is what stops you becoming amazingly impulsive and going on and doing exactly what you want to do. And of course, very often, this control breaks down: people become impulsive. It also breaks down when you become over-anxious and over-depressed. So this is something that works on throughout the course of our development and helps us control our emotions and our basic desire for pleasure. Of course, these systems have evolved to actually drive us to seek the things that aid our survival - primarily food, drink, reproduction, and so forth - but of course, as society has evolved and we have less of these basic needs to concern ourselves with, they could be hijacked by anything that gives you pleasure. These could be anything at all, and as we have become a more leisurely society, we need more and more to find other ways of activating these structures, although of course the primal ones - the sex, drugs and rock 'n' roll - are still high. You cannot just ignore them, even though we have this inhibitory system to try and help us. Somehow or other we have to find things that will stimulate them and that's part of the problem. It is so

deep-set in our evolution over millions and millions of years that we simply cannot ignore this pleasure system.

It was first discovered back in the 1950s by James Olds who discovered these basement pleasure areas in the brain. There are also pain areas as well, although I am only going to talk about pleasure ones. In his experiments, he put metro-electrodes down into a rat's nucleus accumbens area, which allows the rat, when he presses the lever, to deliver electrical stimulation to this part of the brain. It was found that the rat would continue to do this as much as 6,000 presses an hour without satiating - it goes on and on and on. Similar experiments were actually done in the same kind of period of time on humans in the US - on prisoners, as you might expect, trying to get remission. They reported intense pleasure, and it is so intense that basically you ignore everything else - you will not feed yourself, you will not drink, you just spend your whole life stimulating this area. It is an intensely powerful feeling.

If I was to stick you in a magnetic resonance imaging scanner or a PET scanner, and looked at your patterns of brain activation when you were experiencing classical things that we know give pleasure, you'll find a remarkably conserved pattern of activation that occurs. So, if you are shown things that stimulate your interest in sex when you are in the scanner, it will activate the accumbens and the ventral tegmental area, which are the dopamine regions. It is the same for listening to the kinds of music that gives you 'the chills' or the shivers down the spine. This activates the frontal cortex, and also the nucleus accumbens and the ventral tegmental area again.

The pleasure from gambling is something that is causing modern society a problem as well. It can give some interesting insights, because what you find is that if you look at the difference between the period when you are anticipating the event - you know you are going to get it so you are already feeling pleasure - as opposed to when you get it, you find that during the anticipation phase, you actually get activation here of the accumbens, and then during the reward phase you get activation of the frontal cortex. So there is a slight differentiation going on within the system of pleasures that are anticipated as opposed to those that are actually gained. But whatever the experience is, if it is something that causes you pleasure, you will see pretty much the same pattern of activation of these pretty primitive structures in the brain.

There are massive individual differences as to the stimulation derived from different things. Differently arousing stimuli will elicit different levels of intensity of activation of these pleasure centres. One of the big differences you find is in terms of development. So if you look at an adult brain and a teenage brain, you can see that for the same stimulus, the adult brain is very strongly activated, but the teenager's brain is very weakly stimulated in this pleasure area. This seems to be something that is coming through again and again in brain research; that teenagers need a lot more stimulation than adults do to give them the same amount of pleasure, and that is probably why they tend to engage in far more risky-type activities than adults do and it is something one has to bear in mind. There does seem to be some development going on within these pleasure systems which means they are somewhat blunted in early development and you need more stimulation to get the same amount of pleasure.

So we have to stimulate these areas, and, if you like, they are still the same big ones that stimulate us now as they did thousands and thousands of years ago. They tend to come to the fore when there's nothing else in life to control them and life tends to be to the point where hedonism, or type 1 happiness as it is very often called, becomes more and more of an essential. I am not saying you all want these things, but it is a fact that the same things come through again and again. So what do we want? We want to be sexually and socially interactive and perhaps to have insatiable sex drive, provided you actually have the ability to use it. A second one, which is again fairly obvious, is to be able to eat, drink and be merry without any kinds of health consequences. And the third biggie, really perhaps the largest one, is to be happy in some sense and not suffer from any form of anxiety or depression. This is a particularly large problem with modern society - the levels of anxiety, depression, suicide are forever increasing - so the requirement for something like a quick fix to help make us happy is always going to be there.

So, in short, it is to be sexually and socially attractive. Of course, one man's attraction is not another person's - there are enormous variations in what people find attractive in other individuals, and the science of attraction and sex is still very much poking around in the dark, to say the least, but one of the areas I think which has been an expectation, and anticipation, and very much driven of course by industry as well, is that somehow or other there is root 1 to attraction - something you can just spread on yourself and you will be absolutely irresistible to a member of the opposite sex. This is of course purported, one way or another, by pretty much all of the perfume companies - sometimes they are quite obvious about it, sometimes they try to be a lot less so, but nevertheless, that is what is behind a lot of the work that goes

on, trying to understand the smell systems in the brain. There is a good reason to think this because it is a fairly primitive system and you can get information from odours straight through to the parts of the brain that control pleasure and arousal without them actually going through the thinking bits - the cortex. Therefore it is theoretically possible and there are a number of species where pheromones do play that absolute key role in attracting one sex to the other and without them nothing happens. That's not just with insects where we know an awful lot about pheromones; there are also some mammals as well. Notably for example, male hamsters have to have a pheromone from the female in order to actually show sexual response, and, as I will show you in a minute, also male pigs give off a pheromone which is very attractive to female pigs.

I do not know how many of you have read Roald Dahl's 'Switch Bitch,' but it is a series of three stories which includes 'Bitch' where the main character in it gets involved with the development of one of these attractant type pheromones which works on men and so if a woman sprays it on herself, men just cannot resist her. He is something of a renegade and he wants to use this for political purposes and so his idea is to put this substance in a brooch of a rather large lady senator of a certain age while she is having a debate with the President on national TV, and the idea is that by releasing this pheromone in the middle of the debate, the President goes wild and gets impeached. Unfortunately, when putting the brooch on the lady concerned, he broke it himself, and so it had all the effects for himself rather than for the President! But anyway, the idea was that somehow or other this was possible, that you could generate pheromone that would really drive men or women wild, whichever way you wanted to do it.

And yes, they do exist, but only in other species. The key thing is that there are two smell systems in the brain, one of which is the one we all know about - it is the airborne odour system, the smells that you get every day at a distance - but there is also a more primitive system, which is called the nasal system, or Jacobson's organ, which is located in the base of the roof of your mouth, and this responds only to liquid, mainly to liquid-borne odours. This is really the one that responds to these pheromones, particularly contained in urine. Unfortunately though, it does exist in humans, but it has become vestigial; the receptor genes located within the receptors of Jacobson's organ in humans are basically non-functional - they are non-coding genes, so they could not work in this kind of way at all. Nevertheless, that hasn't stopped companies exploiting them.

So, in terms of the market for these things, there is a pig pheromone, which is appropriately called Boar Mate. I can tell you it is very often re-labelled for humans, like this one - 'Turn up the Heat'. It is based on a steroid, androstenone, and it works in pigs, but it has been marketed to humans as well, to turn women on. But frankly, unless you go down to the local pig farm, you are probably not going to get any advantage! There are also ones that women are supposed to put on as well to attract men. I know of one example, 'Romp', which is like a tanning liquid you stick on. I can assure you it is very unlikely to have any effect at all - probably the reverse!

So, so much for smells really! Yes, you can make people attractive and they're pleasant, there's no doubt about that, but in terms of some kind of group 1 aphrodisiac - no, no way.

Foods and plants, we have all heard about. Oysters - great to eat, but actually there is pretty much no evidence whatsoever that they have any impact on the sex drive. There are other herbs, like ginkgo biloba, which is marketed in a male and female versions, but it is still the same herb whichever you have. They have very little effect. The most effective one though is Spanish Fly, though in fact flies have nothing to do with it whatsoever - it comes from a beetle. This one works because it causes a massive irritation of the urinary genital tract. This means that it is very uncomfortable - it is kind of like putting white spirit on you - it just causes burning and that is why it works. So it is not exactly the best way of causing sexual arousal, as you can imagine.

Of course, science will tell you as well that the obvious things - money and gifts - play a very large role in attraction - whether it is money or going down to Tiffany's or I am assured that Manolo Blahnik shoes are particularly important gifts to give to a well-heeled woman.

There is more science going on in terms of matchmaking than perhaps most of us would like to see, especially on the internet. There is quite a lot of science now based behind this, so it is not just putting everybody in a hat and saying, 'Well, do you want to meet them - this is what they say about themselves?' A lot of them are like that, but they are increasingly based on personality questionnaires, such as e-Harmony and chemistry.com. They are based on the fairly well-established scientific evidence from huge numbers of species that it isn't 'opposites attract', it is 'like attracts like', so they tend to match you in terms of your personality. You also get a picture to look at and so forth, and this is all done over the internet.

Helen Fisher has actually gone even further with chemistry.com, in that she takes basic personality types and associates them with particular neurochemical balances involving the serotonin system, the sex-steroid system, and the dopamine system. I will not go into detail, but it is becoming more scientific, and in years to come, maybe we will see how effective this is at finding the right partners for different people. At the minute, what happens is they use the science, but they do not actually say, 'No, this person isn't suited to you' - they will not go that far. They always say everybody has a great match, but behind the whole thing, there is this science and they're collecting data to try to work out who really does attract who.

We have all heard about the actual sex drugs - the sex arousal, sex performance drugs. The big one that almost everyone has heard of, which was a total mistake in terms of its discovery, is of course Viagra. It was developed for a completely other cardiovascular control but was discovered to have an amazing effect particularly in terms of penile erection, causing blood to enter the penis and shutting down the escape of it so that erections lasted for a long time. It was really a fantastic discovery particularly in terms of aging men, but it does not have to be just aging men. Currently in the US, some 23 million men a year take Viagra. It is a \$3.8 billion market at the moment, and it will grow. Five years later, Eli Lilly came out with Cialis which is - will catch Viagra up, mainly because it has a big advantage in that one dose of Cialis will have an effect for 24-36 hours after and it starts after about thirty minutes, whereas Viagra only lasts for two or three hours, again with an effect time of half an hour to an hour - though, it depends, it doesn't work on everybody. There is another one on the market, Levitra, which was also developed at the same time, and that acts rather like Viagra. They all do the same thing and I do not actually know why Cialis has such a long-acting effect compared to the other two. These only affect performance, as it were; they have no effect on sexual arousal as such. Viagra has been shown to have some effect in women - it causes about a 10% increase in vaginal blood flow, which is a fairly minimal effect and really isn't something that is that effective in women. That is a problem, because depending on who you ask, the sexual dysfunction market may be huge in males, but it could equally be very large in women as well.

There is no real independent data for this, but the companies of course have estimated that something like one in five women have some form of sexual dysfunction that could be treated pharmacologically. If you just look at the 'developed' world, that could give you a potential market of fifty million women, so the market could be every bit as big for women as it could be for men. So if anyone comes up with the right potion, then there are billions of dollars to be made. Not surprisingly then, there are some people working on it and products are beginning to appear. The first one has been around now for five years already and it was originally called PT-141. One of my colleagues actually worked on it in animal trials, and I remember him telling me some years ago about it, that it was the only substance he'd ever found that made female rats go absolutely, completely wild in terms of their desire for sex. It has gone way beyond rats now. It is actually delivered now in a nasal spray which is a very good way of getting substances straight into the brain. There is a sort of weak blood/brain barrier at the base of the nose, and that is why you can get drugs of any kind in that way that would not normally go across the blood/brain barrier if you just injected them into yourself. So it is a derivative of a peptide called Melanotan II - it is actually a skin peptide - and it is developed by an American company called Palatin, who also work on anti-obesity drugs, based on the same target receptor. Melanotan II came out in early 2000 and was called the Barbie drug. It was never, ever going to get past the FDA, and the reason for that is because it did everything. It caused you to go brown, so it tanned you; it caused you to lose weight; and it caused you to be very sexually aroused. Everything in one pill will never ever get something like that through the FDA, because you have to have a biomedical concern and a therapeutic angle for this, and this would purely be a recreational drug. So they refined it and that is what PT-141 is, and they have other ones in development which are targeting the obesity side of things. They have done phase two trials on this, so it has been tested in a relatively small number of people. It has been mostly on men to start with - they are going for the established market - and these are some of the comments you get. 'It works pretty well', 'It seemed to be better than Viagra in most cases'. The key thing about it is that it works on the brain; it does not work just on the vascular system, so it is actually making you sexually aroused, and because the parts of the brain that make you sexually aroused also control penile erection, it does both things at the same time. 'With PT-141, you feel good, not only sexually aroused as well, you feel younger and more energetic' - these are all the things that people said when they took it - 'It is having the feeling that you're ready to take your pants off and go.' This is in contrast to Viagra, which doesn't normally create such an amazing impact.

You would have thought that these results would have been good enough, but the FDA are not yet satisfied enough to allow it to progress to phase three trials. They actually cannot really see where the market is that is not already covered by drugs. It has been tried in I think it is about 28 women - this is what this

study was based on - and it has very similar sexual arousal effects in women as in men, but you can quite see why the FDA has certain concerns: for 40.7% it causes nausea and nasal congestion - which is not terribly surprising when you take something via a nasal spray. It seems to actually make headaches worse, which is perhaps exactly the opposite of what you are trying to do. Others suffered vomiting and a whole host of other unpleasant things. But a lot of people would be quite prepared to put up with this, but so far the FDA are not letting it through. It is perhaps a salutary tale that any drugs that have a very pro-sexual effect that come through, the FDA tends to look on them in a fairly negative way, even if they are potential blockbusters.

There is another one coming through. It is in an earlier stage of development. It is Boehringer Ingelheim. This acts also at the level of the brain, primarily on the serotonin system, and again, this is Flibanserin which is also reported to increase female sexual arousal, and they are hoping to go for FDA approval in around 2009. So the market is coming along - drugs are available, though they have side-effects. Of course, if you ever ring up one of these companies, they will tell you they are only for the treatment of sexual dysfunction, but we have already seen what happened with Viagra. As soon as they get released, they go on a huge market which is obviously for recreation as well as the treatment of dysfunction.

There is another compound that I have worked on quite extensively some time ago that is often now referred to as 'the social Viagra', or 'the cuddle hormone', called Oxytocin. This is secreted within the brain to stimulate sexual arousal and bonding. It is also released into the blood to cause uterine contracts and milk ejection for those of it who have heard of it before in women, but it seems to have very pro-social effects in both males and females in both humans and in other species. It is not just in the bonding and the sexual context; a paper that came out in 2005 showed that if you spray Oxytocin up your nose - again, it is a peptide, you cannot just inject into yourself because it will not get to the brain because the blood/brain barrier prevents it - then it increases the trust that you will put in people who are trying to sell you things. The case in the paper was of them trying to make you buy a high risk form of monetary policy, and the higher the risk, you are more likely to trust them if you just spray Oxytocin up your nose. The companies also now marketing this are also claiming that it helps deal with marital spats and all sorts of things where trust plays a big role. It does seem to work as it really does seem to promote trust. It is a very pro-social hormone. It is also being looked at in the context of, for example, treating social disorders, like autism. It could be a very important new target for treatment of effective disorders and so on, but of course it could also be used in a more recreational kind of sense. You can buy this stuff from Verum in the US, 'truth labs', and they do not actually tell you you should put it up your nose; they say to spray it onto yourself and it will work - 'whether you want to be a wow success in the boardroom or the bedroom, this will work!' I have no idea how it could possibly work spraying it under your arms, because it has no smell and it does not get anywhere - even if it gets in through the skin, it is not going to get into the brain. But if, on the other hand, you stick Oxytocin into a nasal delivery - you can get those pretty easily on the market - you might be able to self-administer this.

A recent study has also shown that it improves mind-reading. It is not quite as far-fetched as it sounds. What it means is that you seem to be significantly more able to read the emotional signals that someone who is looking at you are giving, so it is particularly something that you can detect when you're looking at somebody's eyes. Perhaps in a context such as a marital one, this could be a bad thing - it might actually do some significant damage to the marriage; on the other hand, if you are into playing cards, clearly that is going to be a huge advantage in trying to work out who is bluffing and who is not.

Let us move away from sex to the next one, which is, again, a massive issue in the Western world: to be able to eat, drink and be merry, but particularly eat, without any health consequences. We know that obesity is a serious problem in most of the developed countries around the world. Approximately two-thirds of the UK population are in some way overweight or obese, and in Europe as a whole in the last 25 years, the numbers have doubled. In fact, in the UK, they have quadrupled during this time. Overall in the world, the current estimates are that there are around one billion people who are overweight or obese, 700 million are just overweight with a BMI of around sort of 25 to 30, and 300 million are obese, which is a body mass index of over 30. Unfortunately, it is not restricted to adults either. As I am sure again many of you know, an increasing number of children, even under five, are affected, and before anyone immediately says 'Well, there are going to be strong genetic reasons for this' - no, there are not. There are genes, or lack of genes, like leptin, which can cause obesity and which is easily treatable, but you are talking about less than 5% of cases. There are relatively few instances where you can really say there is a genetic causation to obesity.

So what do we want? Well, in Eddie Murphy's 'The Nutty Professor', the professor takes this drug which restructures his DNA in some amazing way, and suddenly you get Eddie Murphy as extremely thin. This is perhaps what people expect biomedical science to be able to come up with - something that would really make you lose all the weight that you put on. But, unfortunately, it is rubbish; it cannot happen.

This is the market-leader at the moment in the anti-obesity line. It was originally developed by Roche and it was called Orlistat and then it is subsequently been called Xenical, and it is available over the counter. It has relatively few side effects, but I will come to the one that is somewhat bothering. It works peripherally; it does not have any effect on the brain. It simply works on your digestive system by blocking absorption of around one-third of the fat that you actually eat. Now, that is fine if you control yourself and you eat as little as you are supposed to. If, on the other hand, you overdo it, it causes mild to moderate gastro-intestine upset. This is the technical term for it, but another way of putting it is that it makes you crap yourself. Literally, it is becoming a social issue, because it is uncontrollable - if you overdo it, then you will suffer this side effect. You can imagine the social impact if this happened to you. So beware, if you do ever take it! You can buy it, as I say, over the counter. It is the only one of its kind you can. It is regarded by the FDA as having relatively few side effects, and this is the one, but it could be seriously embarrassing. GSK are predicting that sales in the next year could reach \$5 billion, so it is a massive drug.

The other drugs on the market are all brain-acting ones. This has been around for a while, Sibutramine or Meridia or Reductil. It is marketed by Abbott. It effects primarily a system in the brain, which is quite important in the hypothalamus in controlling satiety. It seems to act by just reducing your need to eat, but anything that affects this system has blood pressure side effects - hypertension - and so you cannot take it if you have hypertension problems anyway, which a lot of obese people do. It is actually banned in some countries where there have been several deaths, but you can get this in the States and I think you can get it in the UK as well.

The one that perhaps you have heard about more is Rimonabant or Accomplia. It is marketed by the French company, Sanofi Aventis. It affects a different part of the brain; the receptors, which are part of this brain reward system, the dopamine system, and it is present in the areas of the brain that control reward and the idea is that by taking this it antagonises them. You do not feel as much pleasure in terms of anticipating eating. It isn't just eating; when it first came out, it said it offered control for alcoholism, cigarette addiction, and also you being overweight. It is licensed in Europe but of course the market is not that huge for a company in Europe, but unfortunately - it is claimed to help obesity, drinking and smoking - the FDA notably decided not to licence it in the US this year, which was a massive blow to the company and a very massive advantage to GlaxoSmithKline, who now have the whole of the market. Sanofi Aventis were considering that they were going to corner that \$5 billion market which is primarily from the US. So certainly the company will try and get over the FDA, but again, the main issue with it is that they do tend to have side effects which, compared to something like Xenical has a side-effect more serious than just has an embarrassing side effect but not one that's life threatening.

An important point to bare in mind is that all drugs can only be marginally effective, in that the maximum they can ever do is reduce your weight by between 5 and 10%. That is quite important from a biomedical point of view. If you have diabetes, a 10% weight loss can be highly significant in health terms, but it does not equate to making a fat person thin. The reason for it is very simple: there are huge numbers of different chemical systems that are involved in controlling satiety and hunger. As you would expect, this is a terribly important thing for any species to get right. We need to have evolved systems where we can eat more than we need to because of the feast and famine type situation, but most species are normally faced with in a wild environment. Sometimes food is available and sometimes it isn't, so when it is available, you need to be able to take on board as much as possible because you might not get another meal for weeks. But of course we just have to go down the local supermarket. We still have this system though, so we can overeat without any trouble at all and put on calories, but it is a bomb-proof system.

You have many different targets at the periphery, and then there are a whole load at the level of the brain as well. There are probably at least twenty different neuro-chemical compounds that are involved in controlling hunger and satiety, and all the drugs can really do is target one of those or two of them perhaps at a time and not the other 18, and because of the way that biology works, the other 18 compensate for the drug that is effecting just two. So within usually a month or so, they have completely compensated for whatever the drug is doing and that is why there is a solid wall when you get to 10% weight loss, because you've got all these compensatory mechanisms. Yes, we could be very, very clever, we could target fifteen of these, but I can tell you the side effects would be horrible. This is because, at this point, you are affecting basic chemistry in the body and affecting a huge amount of it. It does not just affect digestion and

appetite and so forth; it affects very many other things as well. So the reality of it is that we are not going to come up with drugs that are going to be that effective in the miracle of making fat people thin.

Nor for that matter are the diet companies. The size of the industry again is billions of dollars. In a sense, the size of it proves that what goes off soon comes back on again. If it was that effective, it would not be as big as it is. It is usually worse than before, and if you engage in yoyo dieting, it will also potentially impair your immune system and affect your health. Despite all the hype around the diets, they actually all do the same thing: they just reduce your calorie intake, and that includes the Atkins Diet, as it is now been shown there is nothing miraculous about it at all. So they are simply reducing calories, and at the end of it, you tend to revert to your original bad habits, unless you use that as an excuse to completely change the number of calories you eat every day. Diets can also cause muscle loss, and it is clear the better approach is to adapt your routine and diet slowly, and exercise of course.

And yes, there is a biomedical solution to all this: bariatric surgery is extraordinarily effective as it can cause 70% weight loss. It is life-threatening, it is not exactly the kind of thing you would want to have done to you as it works by restricting the size of your stomach with gastric bonding or gastric bypasses. So, though it does work, I would not recommend it.

The conclusion is that we are not going to come up with miracle drugs that do what perhaps people hope, so unfortunately, eating a lot is one of the hedonistic things that we have to still be careful about. So eat less and exercise more and do not rely on the pharmaceutical.

Well, the final one, which perhaps you would have been expecting me to spend most of my time on, is the drugs that make you feel happy. This was of course epitomised by Aldous Huxley's *Brave New World*, where all the people in the society take this drug Soma, which basically flattens you for most of the time - you are happy - and then you go on Soma holidays where it makes you seriously happy and you have a trip. But it basically controls the whole of society so that no one is ever anxious or depressed, and you can have a drug high if you want.

Arguably, something of this nature has to be considered, given that our lifestyle seems to be having massive effects on our ability to cope. 28 million people in the USA take antidepressants and a huge number do in Europe as well, and it is increasing all the time.

Yes, we have quite a few drugs, and the most notable of the many available for treatment of depression is Prozac, and then you have got cocaine, LSD, heroin, and ecstasy. Are any of these really any good, even if they happen to be illegal?

They all do the same thing: they all stimulate those brain pleasure centres, either directly or indirectly. There is a problem with anything that does that in that there is this thing called a hedonistic treadmill, which is actually more defined in an economic context, one I will come to in a minute, but it is also true of a biological context and is the basis of addiction, which is when it is affecting these reward centres.

PET scans will show the activation of these dopamine receptors in the brain of someone eating the same food who is either normal weight or obese, and the take-home message is that there is a much bigger activation in the normal weight person eating the same amount of food than there is in the obese person. It just shows you that as you have more and more of something, it actually activates those pleasure centres less and less, so you have to have more of it, and that is the basis of addiction. It is extremely simple, and the system works that way.

It seems to also work with happiness as well. I do not necessarily want to stick by these kinds of representations of visions of happiness, but it is almost certainly true. There are measures of increasing income per capita in the US over a period of time, showing that it goes up beautifully, but the measurements of happiness show, if anything, the trend is downwards. So you get more and more, but you seem to be less and less happy as a result of it and this is what is known as the hedonistic treadmill. We reset to the current level: we get something, we expect that, so we want something more, and we want something more, and that is the hedonistic treadmill.

Pretty much all of the drugs affect the classic diffuse systems, the transmitters in the brain: Noradrenaline affecting your tension, mood, sleep, drive and appetite; the dopamine system, which I have mentioned extensively, and which again overlaps the pleasure, appetite and drive; and serotonin, which is particularly acting at the level of the frontal cortex to help control the bad things - obsessions, anxiety, and suicidal thoughts - and that's where Prozac is primarily acting, to help control feelings. So they are all acting on these, in one way or another.

Yes, a lot of us are taking some of these drugs. Obviously Prozac is something you can get prescribed to you, and amazingly, you can actually detect Prozac in our drinking water because so many people are taking it.

There is not a particular rhyme or reason to what is a Class A, B, C drug as opposed to one that is unclassified. The Science Select Committee got experts together to rate the harmfulness of the whole spectrum of drugs that you could possibly get hold of, and that includes our friends alcohol and tobacco, and you will see that alcohol is pretty much up there in terms of harmfulness with your heroins and cocaines, so it is pretty harmful, even compared to the things that we would all think are extremely harmful, like heroin. Tobacco is the same. So there is not a great deal of rhyme or reason to the classification in terms of the harm that drugs do you. We allow some because it is traditional and we always have.

So what is it we need, if anything? Well, we have got the ones I have already mentioned, the ones that we can have pretty much every day in our lives - alcohol, caffeine and nicotine - which are primarily stimulants but they can also, at least with alcohol, be depressants as well when you take too much.

There are the classical psycho-stimulants, cocaine and amphetamines, most of which impair your ability to function; they tend to have cognitive side effects, which can be extremely serious, which is why cocaine in particular is a Class A substance.

You can also have things that depress the system. These make you feel good because you are flattening everything, which could also give you a high - so morphine, heroine, opium, all are in this particular type of category. Again, you are not much good for anything when you are taking them, in terms of functioning in a normal world.

There are the anti-depressants, which work in a variety of ways - the SSRIs and tricyclics - which again tend to flatten you. They cause a level of anhedonia. SSRIs for example are now classically associated with a sort of drop-off in your level of sexual arousal and interest, so it is pretty unlikely that you are going to find anybody attractive when you are taking SSRIs.

There are the so-called psychedelics, which you've all heard about. Sometimes these are now called entheogens which means that they generate a god-like experience and they take you out of yourself. They tend to act indirectly on the brain reward systems, which is why you can both get a good trip and also you can get a bad trip. They do not necessarily activate root one, the pleasure centres, hence LSD is quite a risky thing to take, as is psilocybin or mescaline - they all tend to do the same things. None of these are really hitting at what you would want to do.

There are also dissociatives, which basically dissociate you from reality - again, not the kind of thing you want to do for every day of your life. They tend to hit the glutamine NMDA receptors - Ketamine, PCA, laughing gas or nitrous oxide, Salvinorin-A, which affects the opiate system, and Muscimol, which affects the main inhibitory system in the brain. These are drugs which are pretty dangerous and they impair your functioning in a big way.

Really the only class that you might even consider are empathogens and entactogens, and simply that means they generate feelings of empathy, or they generate sort of feelings inside of tactileness, feeling good. The classic one of these is Ecstasy, first called Adam. This was actually discovered way back in 1912 by a chemist. There are others called GHB. Both Ecstasy and GHB are banned - though GHB was only recently banned in the UK. But also the one I've just mentioned, Oxytocin, which at the moment doesn't really figure in this area at all, and they are pro-social drugs. They make you feel that everybody around you is great. It is very much like Soma, in that sense. So this is, in a sense, what you would want it to do: you would want to feel happy with everybody around you, that you like to be with them, and that you feel good inside. So it is kind of the right route if you want something like this, because you can also function when you are having these things. Of course, if you overdose on them, you can have problems, and it is reported that with Ecstasy, for example, or MDMA (called 'the hug drug'), tends to be best for the first ten times you take it, and then its effects tend to wear off. You mustn't take it with alcohol because it seems to abolish the effect, and it clearly has side effects that we do not want. We have heard about people dying from taking Ecstasy, particularly because there are so many street versions of it that are in some way or another impure.

Liquid Ecstasy is also banned. I think it is probably got a slightly bad press because people think it is related to Rohypnol, the date rape drug, but it does not quite do the same thing. Although, it is a sort of hypnotic and it does tend to promote sleep as well as sexual arousal, so it is potentially capable of being abused in the wrong context. But again, it tends to make you feel good, both socially and sexually, but

again, it has these side effects: if you take too much of it, you could be in trouble, and it can be abused as well.

Oxytocin or things that are derived from around it may be the next potential target. We will try to come up with something that just makes you feel overall that people are nice and the world is great and that you are generally happy. It is pro-social and it makes you feel less anxious. So perhaps new classes of drug that target Oxytocin could be the next generation of a stable form of Ecstasy.

Of course you can get pretty extreme - you can become a wire-head, putting electrodes in the brain, like I originally showed you from James Olds. There is a quote from the Delhi Lama, whom I listened to in fact when he gave his talk at the Society for Neuroscience Congress in 2005: 'If it was possible to become free of negative emotions by a riskless implementation of an electrode, without impairing intelligence and the critical mind, I would be the first patient.' Unfortunately, it would impair you if you put one into the reward centres because you would spend your whole life stimulating them, but there may be some ways of deep brain stimulation.

Of course, as time goes by, there become less invasive ways of stimulating the brain, for instance, transcranial magnetic stimulation. It is been shown that if you stimulate the left side of the frontal cortex, you can make people feel happier, particularly individuals who seem to be resistant to treatment of depression with, for example, Prozac. So yes, it may be possible to end up in a position where you could stimulate your brain when you feel depressed, in a manner not unlike just turning on your MP3 player now.

I have given you a sort of whistle-stop tour of what is out there and what we can possibly achieve. There is nothing of course really available at the minute that you can put it in your tea and you will feel happy; you are going to have to try and derive your happiness from whatever it is you do in your life, and perhaps, for many people, that is the way it should remain. But there is no getting away from the fact we have a problem with people not having a high quality of life, with feeling that they do not and wanting some kind of quick fix for it.

So, at the moment, there is a really pretty good development of drugs that increase sexual arousal and performance. The ones that elicit attraction are, thankfully, far off, but the Oxytocin one does seem to improve things like trust and bonding, which are obviously a key part of relationships.

As I have tried to be as robust as I can, fat-buster drugs are unlikely to achieve anything other than a moderate success, but that could be really important in the health context of course. So the bottom line is always going to be eat less and exercise more.

There are many 'happy drugs' and few of them really are in any way acceptable. Perhaps if we really wanted to develop something like this, it would be potentially a blockbuster drug. It would only be developed in the context of treating affective disorders, but then of course it would again perhaps be capable of being used more generally as a recreational drug, the issue being perhaps to promote pro-social feelings and just a general feeling of wellbeing, but allow you to function quite normally in your everyday life. In time, it might be possible it seems to find appropriate empathogens and entactogens which have relatively few side effects.

There will be the problems of the hedonistic treadmill though. Whatever we do, whatever we give, then you will get used to it and you'll want more, so even if we could stick this thing in your beer or in the water, there still could be a problem down the line that you will just want more or something different, and so perhaps really the answer is always going to be to actually have a lifestyle that generates happiness yourself.

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