Nature, Nurture or Neither? The View from the Genes
Transcript

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Some of you may have come to my lecture, I think it was the last but one. The last one was about incest and the one before was about the evolution of God, and the evolution of God one, I actually introduced with this very useful little slide here, which is an image of a statue that stood on the staircase in the University of Edinburgh Zoology Department, where I was a student, and it is a very useful image because, as you will see, I can use it to introduce a totally different lecture!

What it is, for those of you who did not go to my earlier lecture, well, it is a picture of a chimpanzee. It is called Affe mit Schadel, The Ape with a Skull. It is a German 1950s object and it is a picture of a chimpanzee with a very puzzled expression on its face, sitting on a pile of books, and if you look more carefully - looking at the human skull in its head, you will see that one of the books has the title “Darwin” on the spine, the author, and on the open page, you might just be able to make out the words “Eritis sicut Deus”. Well, all of you of course at Gresham College, I know, it is daily language used in the office, given when it was founded – it is of course Latin – and so I do not need to translate that for you all, but I will for those few who have come who are not expert classicists. It means it is from the Vulgate, it is from the Roman Catholic version of the Bible, Genesis, and it is from the phrase “Eritis sicut Deus”, “Ye shall be like gods, knowing of good and evil,” and it comes from Genesis Book one, where the serpent tempts Eve to eat the fruit of the Tree of Knowledge with that statement – the day ye eat the fruit thereof, ye shall be like gods, knowing of good and evil. Eve, of course, eats the fruit, and Eve and Adam notice immediately that they are unclothed and they then commit the first and least original of all sins, by having sex, and they have children of course, Cain and Abel, God gets understandably annoyed by them and chucks them out into the real world. And actually, in Christian theology, that was the source of original sin. That was the sin that besmirched us all, perhaps the least original of all sins, which is the discovery of sex; we are paying the price now in our own inherited imperfection. Many people see genetics as being a bit like that, a kind of inborn original sin, an imperfection with which we are all marked, not because of some mythic thing that happened 4004 BC, but because of the accumulation of biochemical errors over time, and to some extent, that is true, and that notion of human imperfection is deeply embedded within our psyche. You can see it again and again, not just in the story of the Garden of Eden, but all the way to the present day, when people, for example, believe that intelligence or criminality or wisdom or stupidity or musicality are all embedded in the genes.

The biggest put-down I ever heard to that notion, which really summarises my lecture, I went, a few years ago, to a lecture by Daniel Barenboim, who is a Reith lecturer, and it was a hilarious event because he had not prepared anything at all, and he was being interviewed by Sue Lawley, and she was desperately trying to make the thing go along, and she opened questions to the floor, and somebody stood up and said, “Mr Barenboim, have you ever met somebody like you who was a child prodigy?” and he said, “Oh, no, no, I have never met anybody like me who was a child prodigy, but I have met plenty of their parents.”

[Laughter]

There is a tendency to assume that, actually, we are born the way we are, and that is what I want to explain, the question of disentangling nature from nurture. Can we do that? If we do that, what, if anything, does it tell us about inborn fate?

Well, I start my first-year lectures at UCL, which I have just given my 38th one today in that series, by asking the students to look to the person to their left and the person to their right, and I say – and I say, with some accuracy, that two out of the three of them will die for reasons connected to the genes they carry, and for some reason, they find it funny. I guess they are young enough to find it funny. I guess they are young enough to find it funny. We clearly are not! And that is accurate – quite what that means, I will come back to in a moment. But then I say, “Cheer up, if I had been giving this lecture in Shakespeare’s time, two out of every three of you would be dead already.”

And here are the figures of life and death for children born in England. The chances of making it to be 21, in 1601, when Shakespeare was alive, it was about one in three. In 1801, just before Charles Darwin, eight years
before Darwin was born, it was not much more than one in two. In 2001, it was 98.9%. It is now probably about 99.1%. And of course, we all have to die in the end though. In the old days, we used to die, as this Museum of course will show us, we died from the enemy that came from outside, from cholera, from cold, from starvation, from violence, all these things which really were the plague of London, and in the last five years of course have been utterly banished by Government decree, so they have gone, but now we die, in the words of a now-forgotten politician, “We die from the enemy within”. Things like cancer, diabetes and heart disease all have a strong genetic component, but quite what that means is perhaps rather more subtle than many people think.

Can we separate nature from nurture? Oddly enough, the phrase “Nature or Nurture” is itself a Shakespearean phrase. It comes from the Tempest, and on Prospero’s island, where they are shipwrecked, as of course you know, there lives this awful little monster called Caliban, which the shipwrecked sailors and Prospero himself try to be kind to, and Caliban refuses to listen to them at all and carries on being utterly revolted, and in great exasperation, one of the sailors says to Caliban, “On thy foul nature, nurture will never stick.” In other words, you were born so awful that there is nothing we can do about it. Well, my suggestion is that actually that is a hopelessly naïve view of the way that nature and nurture work – they always work together. It is a maligned view because it actually has led to some very malign political policies.

Here is a chap I always like to show pictures of, Francis Galton. Galton was Charles Darwin’s cousin – I am sure you have heard of him. He left a large sum of money to University College of London in 1911 to found what was then rather embarrassingly called the National Laboratory of Eugenics. We changed the title rather quickly, I have to tell you. He was interested in being well-born, eugenics – that is what it means, and he wrote, in 1871, a book called Hereditary Genius, where he put out the case that actually genius was inherited, as was stupidity, as was anything else you could think of. He worked out, for example, that rowing ability on the Tyne was inherited, the ability to be a boxer was inherited, the ability to be a sea captain was inherited, and of course, that is true to some broad sense. If your father was a sea captain, you are more likely to become a sea captain, and all the way back into history – that is true. But he sort of saw automatically that this was embedded into the very human psyche, it was in the genes, as we would say today, and he was interested overwhelmingly in quality, and he came up with the notion indeed that human quality was in danger of decline because geniuses, people like him, had fewer children than people of lower ability.

I do not want to talk at any length about the eugenics movement, but it was a movement that led to great, vile policies, some of which, the remnants of which are still with us. It led, of course, directly to the horrors of Germany in the 1930s, but people tend to forget that Sweden was equivalently involved in eugenics. Tens of thousands of young people in Sweden were sterilised. In the United States, fewer were sterilised, but you could be sterilised for shoplifting in some states in the United States. It is really rather strange that it never had any influence in Britain. Winston Churchill, in 1917, stood up in the House of Commons and asked for a compulsory sterilisation law, and an MP called Wedgwood, one of the descendants of the great Wedgwood, gave an impassioned account that stated that that was unethical. So, oddly enough, in the home of eugenics, there never was any eugenics, but it turns on this idea that we are born the way we are, and if that is not the way that we ought to be, we should not be allowed to reproduce.

Well, Darwin, his cousin, was a much greater scientist than Galton, and he came up with a phrase which is very useful – I recommend anybody who teaches students to use it constantly – “Ignorance more frequently breeds confidence than does knowledge”. So, if you do not know anything, you can be entirely confident, and Galton, to be frank, knew nothing, and he was entirely confident. The eugenicists of the 1930s knew nothing and they were confident. And I hate to say it, but when the human genome was read off, ten years and more ago now, looking back, we knew nothing, and yet Tony Blair said this is going to change the world. Not! It has not changed the world one tiny bit, or scarcely at all. So, you have to be very careful about what you mean.

So, the idea is still with us. If you go to Google, and you type in the words “scientists find the gene for”, you get something like 38,000 hits, which, given that we have only got about 23,000 genes, is rather a lot. I should point
Here is a Siamese cat which has been kept in a cold room. It is exactly the same mutation of course as the light-coloured cat, or you can keep your cat in a cold room.

You can alter it by breeding from relatively dark Siamese for many generations to make a slightly darker line of any male body, then you can make black pigment. So, the pattern is simultaneously nature and nurture, and it is a pigment, a black dark pigment which we all have, wherever our ancestors come from. Some people have slightly more than others and they have darker skin, but we all have plenty of melanin in our skin and our hair and in our brains and in various other parts of the body, and melanin is made, as most biochemical substances are, in a sort of factory with several machines on an assembly line, and if your factory is working well, you can end up with a black cat. If there is a breakdown in one of the machines in the assembly line, then the stuff gets made and then it is blocked there and you end up with a white cat. So far, so simple.

Now, this particular melanin mutant is certainly genetic. We know exactly where in the melanin pathway things have gone wrong, and if you do breeding experiments and follow simple rules, we know really a great deal about the mutation, and it is a Siamese cat, and we all know about the Siamese cat – they have got a black nose, ear, the nose and the tail, and of course the testicles, which are both literally and metaphorically the coolest part of any male body, then you can make black pigment. So, the pattern is simultaneously nature and nurture, and you can alter it by breeding from relatively dark Siamese for many generations to make a slightly darker line of cat, or from breeding from relatively light Siamese cats for many generations in the hope of making a relatively light-coloured cat, or you can keep your cat in a cold room.

Out that tomatoes have got 26,000 genes. What that says about the ability of the tomato, I do not know. But you can find things like emotional memory, fear, religiosity, sweet tooth, weight gain, language... Premature ejaculation is there – quite how a gene for that would stay in a population I do not know! And there are more and more and more of these, and the idea that they are important is really still very much with us.

How do we know that we have found a gene for something? It might seem obvious, but in fact, it is not – it is a very, very subtle statement. One obvious way that people might think is proof that an attribute is in the DNA, in the genes, is simply that it runs in families, but that is not necessarily true.

Here we have a man with a mild genetic disability in that his ears stick out. He has, as a consolation prize, he is or was Prince Andrew of Greece and of Denmark. He had a son, the Duke of Edinburgh...check out the ears – his ears stick out. He too, the Duke of Edinburgh, had a son, Prince Charles, with his customary look of baffled rage even at the age of five – check out his ears. Prince Charles, of course, had some children. Check out the ears of one of them at least, if not the other. And you might argue, indeed, that that is some kind of evidence that there is a gene in the family which is passed from one generation to the next and half the children inherit it. Yes, well, maybe, and that is a very first hint that there might be genes involved, but inheritance itself certainly does not say anything about genetics or whether it is genetic or not. If you look at Prince Charles’ older son, Prince William, if everything goes according to plan, he, William, will inherit from Charles something which Charles inherited from his parent and all the way back for several hundred years, which are the royal regalia, and they are passed down the generations, following rules as rigid as those of Mendel but there is no genes for crowns. So, the simple statement of finding inheritance is very, very weak. So, something which there is no genes for crowns, there is no genes for wealth, there is no genes for speaking English – we can go on about that.

Here we have a mutation in a cat and there are lots of cat genetics about. In fact, the cat genome, the DNA of the cat, was sequenced about six or seven weeks ago, so we know all about cats, and there are all kind of interesting things in cats. Darwin noticed that all blue-eyed cats are deaf, and he got it right too because all blue-eyed cats are deaf – it has to do with the melanin pigment, and this is a melanin mutation in cats. Now, melanin, of course, is a pigment, a black dark pigment which we all have, wherever our ancestors come from. Some people have slightly more than others and they have darker skin, but we all have plenty of melanin in our skin and our hair and in our brains and in various other parts of the body, and melanin is made, as most biochemical substances are, in a sort of factory with several machines on an assembly line, and if your factory is working well, you can end up with a black cat. If there is a breakdown in one of the machines in the assembly line, then the stuff gets made and then it is blocked there and you end up with a white cat. So far, so simple.

Here we have a Siamese cat which has been kept in a cold room. It is exactly the same mutation of course as the
previous one, but because the temperature has been lower, it can make more black pigment because its surface is colder. If you really want to show off, you can keep your cat in a refrigerator and then you will get a black cat, a very expensive black cat, with a Siamese struggling to get out. If you want a relatively light-coloured Siamese cat, keep it in a warm room – exactly the same mutation again, but this time we have got the opposite effect. It is warm so it cannot make any pigment. There is a famous case of a kitten called Edward, whose proud owner shaved its initial on its side and kept it cold, with a little icepack, and the kitten grew up with the letter E on its side in perfectly natural black far. So, that is a statement that really you cannot separate nature and nurture – they are always intermingled. People often think that it is a bit like eating a cake – you can dissolve what you are, your Siameseness or your intelligence or your criminality, into a slice that is called nature and nurture, a slice that is called nature and another one that is called nurture, but you cannot. You would have to unbake the cake. And you cannot unbake a cake, but you can digest it, and I will come back to that.

There are many, many cases exactly the same as the Siamese cat story in humans. Here is one, which is mildly interesting, to do with a mutation in humans, an enzyme called ACE, Angiotensin-Converting Enzyme, and this is a classic example of nature and nurture in humans. It comes in two flavours. Something like one person in four in this room will have a version that is called the insertion version, and you can see there, it has got inserted into it an extra length of DNA – that is called the I version; and something like one in four, a bit less actually, will have two copies of the shorter version without that red blob stuck into it; and the rest of us will have one of each. Now, ACE is important in many ways – it does many different things in the body, but one of the things it is very much involved in is actually oxygen uptake, and if, for example, you are in some terrible car crash or something like that, then it turns out that your ACE gene is quite important.

If there is some awful accident, like a bus crash or a train crash, and there are 50 people lying around groaning, what doctors do, or the medical system in any country will do, is send in a crash team, as they call it, to deal with this, and they will do triage, sorting - in French, trier- and they sort those who are still alive into three groups: those who are in agony but are not going to die, so they put those on one side; those who are so badly injured that whatever you do to them, they are going to die, so they put those on one side; and then the crucial group are those who are badly injured but if you go in with all guns firing and really work on them, you may save some of them. There are various techniques that people use to do that – looking at the pupils of the eye, for example, asking about patterns of breathing. If you have got what is called Cheyne-Stokes breathing, [gaping], panting like that, you are in more trouble. And a friend of mine, Hugh Montgomery, a trauma surgeon, has been working on the role of this particular gene in those circumstances, and it turns out that, if you have got two copies of the longer form, you are much better with dealing with a low oxygen stress – for example, by your chest being crushed, shall we say – than if you have got two copies of the short form. And it has not yet become standard, but there are now attempts to take to such events a little DNA chip that will tell the doctors within ten minutes what genes the individuals involved have got, and maybe you will pay more attention to the injured people who have got II rather than those who have got DD, who are less likely to survive.

Well, it is an interesting gene, ACE, because it does all kinds of remarkable things. My friend, Hugh Montgomery, is a keen mountain climber, and he is one of these annoying ubermensch – you know, he has climbed higher than anybody else, and he has dived deeper than anybody else, and he has got his own plane, and he has written a million-selling children's book. I am often tempted to strangle him actually... But one of his interests in life is climbing, and he genuinely is, or was – he is slightly older now - but he was one of the world’s top amateur climbers, and he has climbed many, many of the Himalayas, and he has climbed Everest several times. That is before Everest was – you know, Thomas Cook does Everest now, but that was when Everest was still really quite a challenge. But he has never managed to climb it without oxygen, and he began to look into why this was, and he did a survey, a few years ago, asking who are the people who have managed to climb Everest without oxygen, and you can see, if you look at the top version of that graph, on the left, in A, you will see that people who are II, the long version of the gene, are much more likely to have climbed Everest without oxygen than the general population, and people who are DD, the short version of the gene, two copies, are much less likely to do so. There is an irony in this story because it turns out that Hugh Montgomery is in fact DD, so he will never climb up Everest without oxygen. But that is a Siamese cat of an effect – it is nature and nurture. The effect of the gene depends on the environment.

Now, most of us, presumably, have already climbed Everest, with or without oxygen, or do not want to climb Everest, but that has a wider implication. At the bottom there, we have some results from the US Army, and if you join an army – not something I necessarily recommend – obviously one of the first things which you have to experience is some period of intense training, physical training, and one of the things which soldiers do is press-ups. Remember press-ups? Godawful bloody press-ups! I have not done a press-up since I was 16 and I never intend to do another one! But you can do press-ups, and if you are relatively fit person and are relatively young, you can probably, with some effort, do press-ups for a minute or so, but, with training, you may be able to do better. But what is remarkable is that the extent to which you could do better is highly dependent on your ACE
If you look at the lower square there, this is the increase in duration which you can do press-ups for in seconds. So, if you are II, two copies of the long version, you can go on for another minute and 20 seconds, which is really a lot, but if you are DD, I mean, forget it - you can go on for another five seconds. And it can only be a matter of time, it seems to me, before people start screening potential soldiers and potential athletes to ask what is their genotype in this particular case.

However, having said that, of course, it is still absolutely the case that the environment is involved. If you cannot do press-ups, who the hell cares? If you are a nerdy professor like me, we do not do press-ups, thank you very much! Only if you place yourself in an environment where you need a lot of fitness is the gene important.

Here is Mo Farah, perhaps the best athlete in the world. It is not widely known that Mo Farah has an identical twin, and Mo Farah came to Britain with his mother. His twin stayed in Somalia with his father. Mo came to Britain and went to a state school, and was very quickly picked up as having extraordinary athletic abilities, and became what he was, one of the finest athletes in the world. He says that when he and his brother were young, they used to race each other, and sometimes Mo would win, sometimes his brother would win. Now, his brother is a car mechanic, with no interest in sport, and if they were to race each other now, you can be absolutely sure that Mo Farah would win and his brother would not, and that is not dependent on the fact that they share all their genes in common.

So, let us go back to this cake analogy, which I rather leapt into a bit too quick. They are extreme cases - they are single genes with a big effect, but they are irrelevant to most of us. As I have said, many people see one’s attributes - intelligence and the rest - as being like a cake which you can slice into a piece called nature and a piece called nurture. You cannot do that. You would have to un-bake the cake. Or, alternatively, you could digest the cake and that is what digestion basically does: it gets back the carbohydrates and the proteins and the amino acids which are in the cake.

Here is a young lady about to do the experiment. She is about to experiment on this important genetic phenomenon. If you do the experiment too frequently, what happens? You get fat, alright. And I think many of us are aware of this in general terms, but we are now in the middle of an epidemic of ill-health, which is as important as some of the epidemics that spread through the world in the 19th, the 18th, the 17th centuries. It is not the Black Death, but it is a very, very important epidemic, and that is the obesity epidemic. I want to explore that from the point of view of nature and nurture.

I will show you some slides showing the proportion of American adults who are morbidly obese - now, this is 30 pounds overweight for a person who is even shorter than me, 5 foot 4, so that is a lot of extra weight to be carrying for a 5 foot 4 person.

Here, we have got the figures from 1985. Lots of states, in 1985, we did not have the records for, but many we did, and I will go through the years and you will see, as the colours get warmer, you will see what happened in this epidemic. So, we start in 1985, where, the states we have got records for, the majority of them have got fewer than one person in ten who are morbidly obese, and some have got between 10% and 14%.

1990, suddenly, all of a sudden, a majority of states have got people who are obese, about one in eight or more, 10% to 14%.

1995, majority of states, just about, one in six, more than one in six are obese...

2000, we are getting to a situation where plenty of states are moving towards one in five...

2005, some states have got more than one in four...
And by 2010, some states are turning towards one in three...

Now, that is a major, major problem. We will see in a moment that that actually causes lots and lots and lots of health issues, and it is not a local problem. It is a very recent problem – that is what people find shocking. In 1980, it did not exist, and when I lived in the States in the '70s, it scarcely existed. Now, it is everywhere. So, that is only about 40 years or so it has taken to shift the weight of the Americans. Every American puts on a pound a year since 1970 – my God! So, that is what the figures are, and it is not restricted to the United States because, since 1985, a great tsunami of lard has washed across the Atlantic and broken upon European shores. Now, we in Britain have many things to be proud of, and one of the things we should be proudest of is that we are in fact the fattest country in Europe.

Here we have the thinnest, which is Romania. This is a slightly less punitive measure of obesity, and that is understandable. But Switzerland is the second thinnest. Down the bottom here, Rule Britannia, one in four of us are obese on this not quite so stringent measure, and that is well above the average which is, the EU, about 15%.

If you draw a rather more detailed map of British obesity, you end up with this, the fat map of the British Isles, and it is actually quite remarkable because, as you can see, the obesity is concentrated in the poorest parts of Britain – in South Wales, where I come from, in Tyneside, in Manchester and Liverpool. You will see that in the Tory-voting svelte shires around London - you can see that Kent is fat, that is why they vote UKIP - you will see there is very little obesity. So, we actually live in extraordinary times. We live in a time where, for the first time in history, the poor are fat and the rich are thin. So, what is going on – what is this due to?

Well, obviously, in some senses, this is due to a shift in the environment and it is important because it leads to all kinds of health problems. It leads, in particular, to Type 2 diabetes, and Type 2 diabetes is the kind of diabetes that comes on relatively late in life, and it is not like Type 1. Type 1, as we all know, is an inborn ability to make insulin, which was always absolutely lethal, until only about 50 years ago when we began to be able to make insulin and inject it into children. Now, we can make it easily in bacteria, so these children with no insulin live more or less normal lives and that is great. Type 2 is different. It comes on later in life, and it comes on because you become obese, you have too much sugar, effectively, in your bloodstream, and your cells stick up a barrier and say we do not want any more sugar, we have got plenty, thanks very much, so your blood sugar level goes shooting up, and that leads to all kinds of problems. It leads to problems like ulcers on the skin, skin prone to infections – now that is a bit of an understatement. Those ulcers often lead to the amputation of arms or legs as the disease goes on. It leads to muscle problems, heart disease, poorer eyesight, depression, kidney problems, all kinds of problems. A large number of dialysis patients have got Type 2 diabetes.

It is the worst kind of illness to have an epidemic of because it takes a long time to die, to put it roughly. The kind of disease that public health systems love, are things such as heart attacks. They are just great because it is basically a binary system - you are trotting around saying hello clouds, hello sky, one minute, and the next minute, you are dead, so all you have to do is to pay for the ambulance to come and pick you up and that is it. But this is quite different. This comes on in early or middle adulthood and can continue for 30 or 40 years, getting more and more ill until finally you pass away, and the shocking statistic is that one teenager in three in Texas has got signs of early onset diabetes. Now, the US health system is already in a mess, and this is going to ruin it, there is no question.

So, how can we predict what our chances of this condition are? Well, it is actually rather simple. All you need to do is take a tape measure and measure your waist size. Now, it is good that I can talk to this audience because when I am talking to a young audience, I have to say “I am a scientist and I do not use inches,” although actually I cannot think in centimetres at all – I just use inches. So, let us look at men, given that I am a man, and my waist size, I am not particularly proud to say, is…I take 32” trousers, so put me there. If you have a waist circumference just eight inches more, your risk of Type 2 diabetes goes up by 16 times. For women, it is even worse. A slim woman will have a waist size of around 29 or less. If you add eight inches to that, the risk of Type 2 diabetes goes up by 35 times. So, this is a big, big issue, and people are very, very interested in exploring why this has become such an enormous problem.
Well, in some senses, it is of course environmental. The cost of food has dropped dramatically. These are US figures – I have not managed to find the British figures, but the figures are about the same. In the 1930s, the average working man – and it would have been a man in those days – in the US would have to work for about five hours a day in order to get enough money to feed himself, his wife and two children. That has now gone down to about one-and-a-half to two hours a day, so that is because food has got much cheaper. You might argue that is a good thing, but of course the kind of food that got much cheaper is not necessarily such a good thing at all because - again American figures and slightly out-of-date but I have not managed to find any more recent ones – you can see that things like fats and oils, sugars and sweets, and overwhelmingly soft drinks, have got much, much cheaper, and if I took this to 2050, soft drinks would be down here. I mean, if you go to Waitrose, as of course we all do – would not be seen dead anywhere else, would we – you can buy a full fat, as it were, a full sugar litre bottle of Coca Cola for less than some fizzy waters, and that is amazing. There are 26 tablespoons full of sugar in every litre of Coca Cola. The things which have got actually more expensive are things like fresh fruit and vegetables and things of that nature which are actually good for you. So, you could argue that this is entirely environmental, and certainly, to a degree, it is very hard to argue with that, to disagree with that.

However, it is also the case that this runs in families. This is the sugar consumption. Here is a family in which it runs. I think they are probably an American family. Both mother and father are morbidly obese, the daughter going that way rather quickly, and you could argue, well, if it runs in the family, it must be genetic. But no, of course, the proof that it is not genetic is in the next slide because this is a picture of their cat…

[Laughter] (An image of a morbidly obese cat)

It is one of the less familiar facts of modern genetics, and I can assure you it is true, that fat people have fat cats, and they have fat dogs, they have fat goldfish – and that is not because they share genes with their cat, at least I hope they do not. They feed themselves too much, they feed their children too much, and they feed their cat too much, so that is an inherited environmental agent.

We have seen a fat cat. Let us look at a fat mouse. Now, this is an interesting mouse because this mouse has a mutation in a gene which, not surprisingly, is called the obese mutant, and it turned up fifteen years ago in a laboratory stock, and if you have got two copies of this gene, you get morbidly obese, and this animal is morbidly obese. It is kept in its cage, treated well, and it gets as fat as this.

Very occasionally, children are born with this condition, and here we have a picture of a young boy missing the hormone involved. It is a hormonal thing called leptin. That young boy, as you can see, is missing the hormone. On the left, that is before treatment, and afterwards, he has been injected, given leptin treatment and is more or less cured.

Leptin is what we call a satiety hormone. We are all familiar with the sensation of hunger, and that is a hormonal sensation. I have to say, I am enjoined by my employers at UCL to put in an advertising break every half an hour into my lectures about how wonderful UCL is, and in fact, the very first hormones were discovered at UCL and they were appetite hormones. So, insulin is an appetite hormone. When your blood sugar drops, insulin tells you “Go out and get a cheeseburger”, “Go out and get a Coca Cola”, and you do it. But less familiar is the notion of satiety, that you go and get your cheeseburger, and you might even have two cheesesburgers, but you do not have ten because you have a separate series of hormones, leptin being one of them, and there are others called ghrelin and the like, which say, enough is enough, you do not want any more food. This bloke, this kid, and the mouse, are missing leptin, so if there is any food – they are hungry all the time, and this boy, without question, it is hellish for their parents because their baby is genuinely starving hungry all the time, and screams and begs for food, and it is very hard to turn him down, and that is because he perceives himself as not having eaten enough. But this is only important where there is plenty of food. For a wild mouse, for example, it does not live in a nice warm laboratory cage with tons of food. If you have got a leptin deficiency, it does not make any difference because you are not going to be able to find enough food to get fat. If you were to go back to the days of hunger in Britain, it would be just the same. If you had leptin deficiency, too bad – you would be hungry, but you would stay hungry because you would not find enough food. So, it is a nature/nature thing.

However, things in the last couple of years have become rather more tangled. Here is a mutation in a mouse. It is the Prince Charles mutation to some extent because check out his ears…but I’m not going to particularly talk
about the ears. I am going to talk about another mutation which our friend Mickey, widely used to sell junk food, needless to say, our friend Mickey has got this mutant. If you look at his hands, he has only got three fingers and a thumb on each hand, and presumably, although he is rather shy about his feet, he has only got three toes and a big toe on his feet. There is a mutation in mice, called FTO, which stands, plonkingly, for fused toes, and if you have got this mutation in mice, your toes fuse together. So, big deal, I hear you say.

If you find the mutation in mice or any other creature - you can search for it and find it very readily in the human genome. It would take you five seconds. You type it in and there it is, we have the same gene, and we have the same error as what causes fused toes in mice, but bizarrely, in humans, the fused toes error in mice does something completely different because it is an appetite gene. That just reminds me how little we know about genetics. What the hell is going on there, nobody knows! So, about a third of the people in this room have got two copies of the amino acid...the DNA base called A, at a particular site in this really rather large gene, just one DNA change. About a third, or a bit less actually, have got two copies of T, and the rest of us are intermediate. Now, if you are AA, you weigh, on average, about two kilograms more than somebody like me who is TT. So, this gene was discovered and people assumed that it was something to do with your digestive system and so on, but it is not. It is actually a gene that is active like many others involved in this issue, and that is just one of many such genes that we now know. Where are they active? They are active in the brain. We know of many genes like this now. They do not work in the digestive system, they work in the brain, and that is where the issue is – it is appetite. Some people, quite genuinely, have a much bigger appetite than others, and in an environment where they can satisfy that appetite, they are at much, much greater danger of obesity. So, the cure, if there is a cure, is to eat less.

I remember Sydney Brenner, who was the cleverest of the Watson, Crick, Brenner, Benzer group, I mean, Brenner has got a brain like a planet. He is still around. Sydney was telling me once, “You know, they say they have found the gene for obesity – I know what the gene for obesity is, have known for years. It is the one that makes you open your mouth!” He was dead right. We did not realise how right he was, but that is what it is, it is a hunger gene. So, that is what lies behind this particular, very important, epidemic: the gene, which has been around for years, now is in an environment where those at risk can actually succumb to the risk, become obese, get diabetes, and die young. Now, that actually kind of argument happens again and again, and I do not want to keep repeating the case.

Let me talk briefly about one of Galton’s real obsessions which had to do with crime... Francis Galton - if you ever see the phrase in a scientific paper “It is easy to show that...” you know there is something very weird going on, because nothing is easy to show. Galton was convinced that it was easy to show that the criminal nature tends to be inherited, and in some senses, he is certainly right because the strongest predictor that a boy will go, or a person will go to prison is if his or her father has been to prison, and in that sense, clearly, it is inherited. But, clearly again, it is not quite as simple as that.

So, that is Galton’s statement. Galton did all kinds of strange things. These are Galton’s composite photographs, and what Galton did was get a whole pile of burglars and a whole pile of muggers and a whole pile of cheque-fraud, of plastic card cheats, and take pictures of them with an early camera and print them altogether on the same plate – the first person to do that, a composite picture. He hoped he would get an ideal burglar and an ideal mugger, but, as you can see, it did not really work. They all just look like thugs really. And he had the decency to say it did not work.

But that argument has gone much, much further now, and here is one of the ways in which genetics has played a part in it. Here we have an example of what I sometimes think of as molecular phrenology, phrenology being of course feeling your bumps to see whether you are musical or whether you are a criminal and so on. Now, we just feel the bumps but we use very, very expensive machines to scan the brain and effectively do the same thing, and there is a lot of very strange stuff goes on: you know, if you think holy thoughts, this bit lights up; if you think sexual thoughts, that bit lights up; if you listen to Mozart, this bit; if you listen to the Sex Pistols, that bit – you know, it is all a bit strange. But many of those things are very, very hoaky indeed, although lots of money is being spent on it.

But one of them which is probably quite dependable turns on this little segment at the base of the brain called the amygdala, and that actually means it is a nut, an amygdala. It is sometimes rather foolishly called the lizard brain, the primitive part of the brain, deep down below the conscious part, which is the cortex at the top. What the amygdala does is light up under conditions which are alarming, and we know that because of a series of
experiments which really, I would say, were not ethical, but people did them anyway, and probably would not get away with them now, which was to get a pile of students and pay them some sum of money, 20 quid, to sit in one of these machines and have their brain scanned. And you tell the students, “Well, we are going to do a scan of your brain to see whether different parts of your brain respond to, shall we say, different flower colours – so we are going to show you a rose, we are going to show you a dandelion, we are going to show you an apple flower, we are going to show you a magnolia flower, and we are just going to look at your brain and you just think about these flowers.” The student’s lying there, with this machine, making a terrible noise, going round his head, thinking, “Oh God this is boring - at least I am getting paid!” and then suddenly, without any warning, is inserted a picture of some horrible event, somebody being decapitated or a terrible car crash or somebody with an awful deformity, with no warning at all, and then the poor student immediately thinks, “Oh my God, what was that? That is not a flower! Jesus Christ!” and what happens is that the amygdala lights up. The extent to which it lights up is shown here, from scarcely any lighting up to a lot of lighting up, and here we go, different pictures of the same thing, and it turns out that the extent to which it does this depends on a particular systemogenic variation which is certainly, like the obesity thing, is certainly present in this room.

It turns on the activity of a particular variant, an enzyme called MAOA, monoamine oxidase A. To put it crudely – and we know more about it than this – it comes in two flavours. Let us just look at the males here. It comes in people with – some people have very low monoamine oxidase A activity, some people have very high monoamine oxidase A activity, and if you zap people with this nasty shock, this picture of the decapitation, and you look at the extent to which that part of the brain lights up, there is a dramatic difference between those with the low activity and those with high. If you have got low activity, you have much more of a response, much more of a sudden response of horror and emotion when you see this than if you have high activity. I can tell you that I myself have very low MAOA activity, so no difficult questions please - you might regret it.

And I know that in several ways. One of the ways – and some of you may share my problem – I find it very difficult to drink red wine because if I do, I have dreadful nightmares and sometimes I shake. I find it impossible to eat soft cheese for the same reason – I do not eat cheese at all, simply because it makes me sweat and makes me feel tense, and that is a well-known phenomenon. There are certain antidepressants, for example, which, if you take them, and I do not, you are told not to drink red wine and eat soft cheese because it has to do with this monoamine oxidase enzyme, which is involved in breaking stuff called thylamine down. But I know the effects on emotion in a different, and rather alarming, way.

More than twenty years ago now, when I first moved into our house in Camden Town, I was walking up on a lovely May evening, up the little few steps to the house, and I was attacked from behind by two guys who started beating me up, and I thought this is very irritating, and I went completely crazy. To my horror, I went completely mad. I hit one of them and I hit him hard on the nose, broke his nose, broke my finger, it still remains broken, and then went completely apeshit, screamed and yelled and chased them down the road, yelling “Stop them! Stop them!” and was joined by somebody else, and then we went past a bus queue and they all looked at us and I said “Get them!” and then they disappeared and it all ended in fiasco. The next morning – and I was badly shaken, I was genuinely badly shaken. I went to hospital, was bound up, came back, and I was badly shaken, and the next morning, to my horror and dismay, I was still pretty shaken, I was going to work, and I thought, ah, tell you what, I will pick up this kitchen knife, and if I see one of those guys, I will kill them… and I thought what the hell are you doing, you know?! What the hell are you doing?! So, I put it down and calmed down, and I have not broken anybody’s nose since, in spite of the difficult questions that they insist on asking me.

And that is a real phenomenon, and this phenomenon, having a low activity in this gene, has been used, or at least people have tried to use it, in criminal cases. There is a famous case you may have heard of, many years ago, 1993, Stephen Mobley, who was a murderer in the States, and in the States, in the late-1970s, the death penalty was brought back, and different states of the union used different trial mechanisms, and the state of Georgia, where Mobley had killed several people – he was a dreadful man. He was a guy who attacked Domino pizza shops with a pistol in Atlanta, Georgia and people behind the counter are told, if anybody holds you up, give them the money, and so they gave him the money, but what Mobley did was just kill them anyway, and he killed at least five people. He was very quickly picked up and imprisoned and charged with multiple murder, and he was found – and he admitted it, he was clearly guilty, was found guilty. But the state of Georgia had a very rather odd system, whereby there were two trials: there was the guilt phase trial; and the penalty phase trial. The guilt phase trial, in this case, was straightforward – it was absolutely clearly that he was guilty. But then came the penalty phase, and the penalty phase is with a different jury and a different judge who decides whether or not the death penalty should be applied.
It so happened that at just that time a paper appeared in the journal *Science*, which became very notorious and you may remember it perhaps, about this particular system of variation, monoamine oxidase A, to do with a Dutch family, in Nijmegen in Holland, where they did not just have low activity, they had no activity of this enzyme, and many of the young men in this Dutch family with no activity had got into terrible trouble with the law - they had set fire to buildings, they had stabbed people, they had been in dreadful fights. And Mobley’s attorneys actually rang me up – God knows why they rang me up – about this paper and said we are going to use this as a defence, “It was not me that did it, it was my DNA.” This led to a big shock to the American legal system because it is a kind of defence. It is a defence. If you hear voices that tell you to murder that man because he is the devil, they will treat you differently than if you decide to murder that man in order to steal his Rolex watch. So, it seemed that there might be something in this, and it went on and on and it is a long, long story, and after about six months of the trial going on, Mobley’s father, who was paying his lawyers, suddenly realised that if his son was a criminal because of his genes, no monoamine oxidase A, he must have inherited it from his father, and that was libellous, so he sued his son’s lawyers for libelling him, the father, and the lawyers were just completely amazed by this, and so they walked off the case and said, “Well, to hell with you – we are not going to go along with this,” and Mobley, in the end, disastrously, because I hate the death penalty, was executed.

So, you might say, that is a very strange thing that there is a gene for crime. It would be simplistic to say there is a gene for crime, but of course there is a gene that predisposes towards crime for those people who are unlucky enough to inherit it. It makes a hormone – called testosterone. We all have testosterone, while we may not know it, both men and women, but men have much more. Women have small amounts of testosterone, which is why elderly ladies sometimes grow rather charming moustaches – that is the testosterone. But men have much more, and testosterone is dangerous stuff.

Some bodybuilders inject themselves with testosterone to make themselves more into an ideal male, with big hefty muscles. But if you do that and you inject testosterone, your life expectancy drops quite strikingly. You are much more liable to be killed in car crashes, in fights, to be murdered, to commit suicide – all these male things happen much more among testosterone abusers. But it is true also for the men among us.

Here are the patterns of life and death for men and women at different ages. As you can see, from 0 to 80 is the mortality rate, up the vertical axis, and at the top left, you can see, men in blue, women in red, men die at a higher rate than women at all ages. You can dissect that a bit. If you look at the bottom left, accidental deaths, men die in accidents at a much higher rate than women do. Four year old boys are killed in accidents at twice the rate of four year old girls, and the effect gets even more striking when you get to be a young adult. It is the case, and many people dispute this but it is in fact true, that men are struck by lightning at three times the rate of four year old girls, and the effect gets even more striking when you get to be a young adult. It is the case, and many people dispute this but it is in fact true, that men are struck by lightning at three times the rate of women, and that is not because there is a gene that attracts thunderbolts, that is because they do those male things about going onto a golf course with a lightning conductor in their hand, or climbing up a mountain to show how masculine they are, and zap, they get hit.

Interestingly, on the bottom right there, men are much less good at dealing with parasitic and infectious diseases because one of the effects of testosterone is to suppress the immune system. That, rather in brackets, is why women have more autoimmune diseases where the immune system turns upon itself, like multiple sclerosis.

And, most of all, men are murdered much more than women are, but men get their own back because they murder much more than women do. Here is the murder rate in England and Wales, men in red this time, just to be awkward, women in blue, and you can see that the murder rate by men is ten times what it is by women. It peaks at about the time when a young man is trying to show what a wonderful husband he would make, at the age of 25, or trying to get rid of the opposition. And that 10 times difference is universal. The murder rate across the world varies by 100 times, from Singapore where it is very low, to Honduras where it is 100 times more common, but it is still ten times different between men and women. For example, in the city of Detroit, we have exactly the same pattern, although elderly men are grumpier. So, you might say, well, here we have the gene for murder, for crime, and you would be absolutely right – you definitely do have the gene for murder and for crime. The murder rate per million per year in Detroit goes up to 1,000; the murder rate per million per year in the United Kingdom is between 20 and 25 – it has come down from these figures now. So what that is telling you is that a particular gene predisposes those men, as we call them, to violence, but it only manifests itself, like the Siamese cat, in a certain environment. If you are in an environment like Detroit, where you are surrounded by poverty, by drugs, by gangs, by police brutality, all of these things, then there will be a massive murder rate. If you are in somewhere like Britain, and even more so in Singapore, which is a relatively equitable society, that is much more likely. So, we have got a situation then that some people, because of their own heritage, are at more danger of becoming murderers and being murdered because of the environment in which they live.
So, that really tells you that the idea that you can separate out nature and nurture for murder, or anything else, is completely foolish, or, to put it in a broader context, it also tells you that science will tell you everything you need to know about yourself, apart from the interesting stuff.

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