

TODAY'S NEUROSCIENCE, TOMORROW'S HISTORY

A Video Archive Project

Professor Uta Frith

Interviewed by Richard Thomas

Supported by the Wellcome Trust, Grant no: 080160/Z/06/Z to Dr Tilli Tansey, Wellcome Trust Centre for the History of Medicine, UCL, and Professor Leslie Iversen, Department of Pharmacology, University of Oxford.

Interview Transcript

Early years and influences

I grew up in the Rhineland Palatinate, which is an area very close to the French border. I grew up in the town called Kaiserslautern, which was famous only for one thing: football. And I went to university in Saarbrücken. I had no idea when I went to university what I would actually be studying. I had very wide interests. I wanted to really learn everything: different languages, learn about cultures, learn about history, and I very seriously studied history of art, but I was also very curious about this subject psychology. And I thought well, let's have a look; let's see what they are doing there. And I was captured.

I went to London for the first time in order just to have an immersion language course, probably only for a couple of weeks. And I have to say, I absolutely loved being here: it was a very, very different world. It was very different. This was in the early sixties. And I thought, "I must come back and study here – not Paris."

And I think a very important influence on this decision was not just the language, and the very nice way of life, which I really adored, but the fact that I was very interested in the books by Hans Jurgen Eysenck. He wrote books that were called *Uses and Misuses of Psychology* or *Sense and Nonsense in Psychology*, that kind of title, and they appealed to me enormously because they were the kind of books that really rubbished all the very crazy ideas about, well, to some extent, also they rubbished psychoanalysis, and ideas that were at the time still very fashionable but didn't seem to have a scientific basis.

London and a PhD at the Institute of Psychiatry

So, I knew somehow, that what I really wanted to do is a PhD: to learn how to do research, how to find out these questions. So then, by accident, I think, I found that there were these amazingly interesting children, the autistic children, to study. And by another incredibly amazing accident, I found that *the* authorities, the people who did the most exciting research in the field, were actually at this very same institution: the Institute of Psychiatry. And this I found out completely by accident because I read one of their papers – this is, I’m talking about Neil O’Connor and Beate Hermelin. I chose a paper for our journal club – that’s what students do, of course – every week you have something new to discuss. And there was this paper, and somebody said to me, “Do you realise that the authors of this paper are actually here at the Institute of Psychiatry?” I was really delighted, and they were pointed out to me in the canteen, and I very timidly approached them and said, “You know, I’m a student, I’ve read your paper: could I talk to you?” And they were very approachable and immediately invited me to visit them in their department, where they did this wonderful research, and I found out a little bit more about they were doing, and it just struck me as the most wonderful thing that I could possibly be doing, to do more work in this area. And I was delighted when Beate Hermelin said, “Why don’t you come and do a PhD with us?” So, I did.

They insisted on having elegant, economical experiments. Being influenced by general psychology and being very rigorous, very, very rigorous in the kinds of controls that you had to do. But they were not very encouraging as to building big theories, either on the basis of the results or regardless of the results. They were rather cynical, in fact, about the big theories. And it took John Morton, I think, to explain to me that you should not be so cynical about theories, you should not be disdainful about them; that unless you could predict what you are finding in an experiment, rather than just describe it, and you can predict it only from a very good theory, you really did not have very satisfactory progress, because you were just randomly finding facts that were more or less interesting. But they would be related to an important big whole. So he actually insisted that I would think in a theoretical way, which took me some time, I think, to get used to. And I tried it first out in relation to understanding the development of reading and spelling.

Dyslexia – first theories and insights into its cause

It’s a very interesting question that you could have a congenital disorder of reading, because reading, after all, is a supreme cultural activity. It’s something that hasn’t been around for more than about, well, five thousand years at the very most, and then of course its been around as a pretty universal skill only for about a hundred years, if that. So it’s really astonishing to think that the brain has something to do with it, because the brain in terms of

its long, long, long evolution cannot have been built in order to read in the way we read. So reading is something that capitalises on something else that the brain is very good at and has evolved over millions and millions of years, and this is speech and language because the text that we read is of course visible language, but it is language. And this was a very deep insight, I think, that came to people who thought about what is necessary in order to read.

So at the very beginning, when I started to be interested in reading and reading difficulties, there was a very strong ideology that dyslexia didn't exist at all. It wasn't to be taken as a brain-based condition, but it was something that was completely artificial, that was perhaps the result of lack of interest, that was perhaps the result of bad teaching, or it was actually something that middle-class parents would like to invent for their children if they didn't succeed at school. Because they couldn't possibly think that ordinary, intelligent children couldn't learn to read and spell. Now I thought, "Yes, very intelligent children may fail to learn to read and spell for some very, very specific reason, for the kind of reason that makes it also impossible for adults after brain damage to read and spell." Now the question was, "What was it? What should one be looking at?" And I think the first idea that seemed very tempting because, after all reading is a very visual activity that one should think of it possibly as a visual disorder.

It took, I think, Maggie Snowling, who came to me as my first PhD student, and was extremely interested in understanding dyslexia, to really come to this insight with her work, with her experience and her experiments, that the problem is actually one of hearing rather than of seeing. And not hearing in general, but hearing and saying little speech sounds that map onto letters. So we have the code of sound to letter, which is so central for the alphabetic writing system, which is difficult to grasp for some people, and these are the dyslexics.

Dyslexia – speech processing and the spoonerisms test

A phonological deficit is really still a pretty vague term to indicate some kind of problem in the speech processing system, and phonology is really a way of combining speech sounds in different ways. This is what the letters of the alphabet capitalise on. It's not something that we are aware of. We just speak without thinking about it. It's one continuous stream of words. But actually, there are all these little speech sounds that have to be accessed very quickly, and we only are aware sometimes when we make mistakes, that there are very, very complicated processing processes at work. And in dyslexics, these processes are not working as well as others. So this is what we were trying to investigate, especially with adults, with adult dyslexics who had, in fact, learned to read and write very well. Many of

them compensated excessively well, so that if you gave them a reading test and a spelling test, they would come out as perfectly fine as average for the population. These were people who were actually university students. And many people would have said we cannot call them dyslexic any longer, because by the criteria for reading and spelling tests, they are not really abnormally inaccurate or don't have the ability as other children. But we believed of course, that their speech processing would still show these problems even when they had compensated for the other difficulties and the kinds of tests that we came up with for the adults has something to do with manipulating speech sounds in the head. So for example, there is a test of spoonerisms. So this is a very easy thing to do: you have two words and you have to swap the beginning sound of each word and put it in a different place. So you have 'lemon basket' and you make 'bemon lasket' out of this. So we had a little test like this. For example, 'John Lennon – Lohn Jennon'; 'Helen Mirren – Melen Hirren'; 'Kylie Minogue – Mylie Kinogue'. This kind of test shows remarkably well when people have difficulties manipulating speech sounds, so dyslexics find this really hard. They take a long time to think over this, and other people can do it absolutely very, very fast. So it's a question of how many can you get correct in one minute, for example. The very severe dyslexics can't do the test at all. This is just one of the whole battery of tests that have to do with speech sound manipulation.

Dyslexia – visualising brain activity during speech processing

We now really need to know what this phonological deficit is; how it can be broken up into different components; and we need to know how often this actually occurs in a very pure form in individuals. What is much more likely, what is actually seen in the clinic is that you have superimpositions of all sorts of problems together and they are the typical picture that you find. For example, attention deficit together with dyslexia, and we need to know why they occur together.

So the progress that has become possible only in the last ten years or so, is to look at the living brain using neuro-imaging methods. So this was the wonderful challenge to say, "Can you test your hypotheses?" For example, the hypothesis about a phonological deficit by looking at the brains of dyslexics and non-dyslexics while they look at print, for example, or while they do other things like recall phonological tasks, while they name, for example, pictures. Now the outcome of this work, and this is still work very much at the beginning, because we need much more than ten years of work to know what is actually going on, is that indeed it is the left hemisphere of the brain where all the language speech processing is happening, where we find the biggest differences between the dyslexic brains and the normal reading brains.

And we can actually see, demonstrate, in a very nice visual form, which is what the neuro-imaging techniques allow us to do, that there is a disconnection between certain components of this speech processing system in dyslexia that we do not find in the normal reading brain. And it seems to be the case that there is one region, which is very much at the back of the brain, and underneath the temporal, a particular area which has been called the word-form area, or it has been known as Brodmann Area 37, and this area seems to be the one that gives a very different signal when you compare the dyslexic brain and the normal brain. And it is reduced in the dyslexic brain, as if there is just not as much information being collected there in the end to recognise words, and to access names of words, to be able to very quickly say how a word is sounded; or even what the name of a picture is.

Now, clearly this is still very much in need of exploration, and one of the particularly exciting things that we can do with these techniques, is to find out how compensation and special tuition and remedial education, helps a dyslexic to overcome their difficulties.

Dyslexia – the English language and dyslexia in Europe

I have been very aware of the special complexities and difficulties of English grammar. It always seemed to me a kind of writing system that would be particularly difficult to cope with if you were dyslexic. While, in a language such as German, you have much better means of overcoming the difficulties because it's relatively regular. And even more so in Italian where you have a writing system that is so utterly transparent that almost anybody can just pronounce the words that they've never seen. Italian children are usually able to learn to read very well, very accurately, after one year at school. But in English schools, we all know that there is a huge variety there: there are those who lag behind for a very long time, and it takes at least three years until all the children are at a reasonable standard that they can compete with these Italian children. So I did think that it must have some implication for dyslexia, and my colleagues in Italy and also in France, were very interested in comparing the kinds of tests that we had used with English dyslexics, trying them with Italian and French dyslexics.

So, we started in the mid-nineties to do this work, and I think the first papers started to be published in about 2000. It took us a very long time to carry out. It was funded by European sources, because we thought it really was very important to find out the differences -- the cultural differences -- that contribute to the ability to learn to read and write, and to use written language. These things have great implications for career choice and development. They have economic implications.

So the first really important problem we came across is, if we want to find dyslexics in Italy, where are they? There are hardly any. Of course, does that mean that maybe dyslexia is really a culturally specific disorder? This would be completely incompatible with the idea that it's a neurological disorder, which, in relatively similar places and countries, should probably occur to the same extent. So it was very tricky to find these dyslexics in Italy. But my colleague, Eraldo Paulesu, had a way of finding these people by testing hundreds, hundreds of students in group tests under difficult conditions. He used the test, for example, of the spoonerisms, and sorted out again the very worst performers in this group. And so he whittled them down until he came to a group that really were just the like the English dyslexics, just like the French dyslexics. And when we looked at their brain processes, they showed exactly the same differences to their Italian controls as did the French dyslexics, as did the English dyslexics.

Dyslexia – does it run in families?

The suspicion that dyslexia was actually to do with a genetic fault, a genetic predisposition was a very, very surprising one because most people would think that this is surely very unlikely. We're talking about this artificial skill of reading which has to do with schools and teachers, so how could it have to do with anything with genes? But it was quite clear from twin studies, from family studies, from pedigree studies, that yes, it is something that did run in families. And people were encouraged therefore to look for a genetic basis. And earlier than some other disorders, people were very enthusiastic, and suggested various possible genetic mechanisms that could lead to a subtly different development of the brain. But I have to say that even now, we are not at a final answer of this. This has turned out to be much, much more difficult than was at first thought. We are convinced though, from the fact that dyslexia runs in families and it's, it's a well-known fact that if one of your parents are dyslexic you really have a very high chance to be dyslexic yourself. So you must assume a genetic contribution is there.

Autism – a disorder of behaviour or biology?

I was a very young and ignorant, naive student, who was actually still struggling to learn English, but I was completely fascinated by being able to study face to face, children with autism. This was the very first time I had ever heard of autism or childhood psychosis. We didn't quite know how to call these children at those times. I was completely, completely amazed that they existed at all. That they existed in the sense that they were so beautiful, so graceful in many ways; that they could do so many clever things, and yet that they had absolutely no way of relating to people, of communicating, of even being interested in

capturing an adult's attention or another child to play with that child. They seemed to be completely in their own world, and it really made me think, "I would love to find out how this is possible; how such a mind could be developing in exactly this way, which gave these complete paradoxes with some things working so well and other things not at all".

Autism of course is the condition that must have been around as long as humans have been around. But it's a condition that hadn't been given a name, hadn't been given a label until Leo Kanner came along, and almost at the same time, Hans Asperger. So these two men were the first to not just identify children with autism, but also using the name autism. We're talking about the early 1940s. But just afterwards, in child psychiatry and psychology, there was a great fashion for psychodynamic, psychogenic explanations, and a very strong tendency existed at that time to think of autism as a psychogenic disorder, something that was due to extremely disturbed relationships between mother and child. Actually, something that was of a totally external and social origin and the brain just didn't come into it. That, that was the way psychology was perceived at the time. And it took a while. It took till the early 60s until some people were actually brave enough to think of the biological origins, and actually to really want to describe what autism was like. And I would say that my mentors, Neil O'Connor and Beate Hermelin, were absolutely pioneers in this respect. They tried to find out whether autistic children were in any way different, in terms of their cognitive, emotional, social abilities, from children with other types of mental disability. And they conducted the most elegant, simple experiments showing that indeed, this was a group that could be distinguished from the others.

Autism – the information processing revolution

My experiments in the sixties and early seventies were very strongly influenced by the revolution that happened in cognitive psychology at the time, that is often referred to as the information processing revolution. So we looked at perception in a different way from how people had looked at it before. We were trying to think of patterns that might be in the environment, that were simple or that were complex, that had information in them or noise in them; that were random or not. And I thought at the time that it would be quite interesting to see how much of this information the children with autism extracted, and indeed also how much pattern they imposed. This was a very interesting question for me because I had observed the very strong stereotypic and repetitive behaviours that had been one of the major diagnostic criterias of autism since Kanner first described it. So, I found in these experiments that indeed, the ability to extract patterns in spoken language or in visual features in the environment was less good than in the normal children. But the tendency to impose quite rigid patterns from the inside was very high in the children. And this was

something that opened up possibilities to think of downstream effects on, for example, language or perception or strange kinds of movement patterns.

It seemed from the experiments that were done on all these stages of information processing, it was the central coding that was really the critical factor. That's the huge black box where we knew very, very little about. But that's where the problem was in autism. So my studies in my PhD on pattern perception and pattern imposition compelled me to think that there was a lack of meaning. It was as if meaning was not sought in the same way as in ordinary children. And this was shown in the way that language was used, which seemed rather meaningless chatterings, repetitions; and in the way play was used. There was no meaning there in the sense that it was a kind of role-play or social play. So it seemed to me that there was a crucial problem there. In addition, it was quite clear that the key feature of autism, which Kanner had described as 'aloofness', had something to do with a lack of communication, a lack of desire to communicate, which was very, very odd because it wasn't clear that this was a motivational failure in general because sometimes the children would do tasks incredibly well, and showed very high ability, if they could understand what the experimenter was actually wanting them to do. But it seemed that you had to leave it to the materials to evoke this ability, you couldn't actually tell the child in some way, "This is what I want you to do".

Autism – theory of mind and the Sally-Ann experiment

Well, I think there was at the end of the seventies a general dissatisfaction with how much we could achieve through nicely designed psychological experiments. How much we could actually understand about autism, because in some sense they failed to deliver. They didn't tell us why these children had these peculiar difficulties in social communication. It wasn't a language difficulty, which was in fact, in a way, the best bet up till that time and it wasn't a difficulty that we could get a handle on in this central system. So it was necessary to look for different ideas in different fields and of course, there were lots of interesting events happening, interesting papers. And one of the interesting papers that I came across was the paper by Premack and Woodruff, which was entitled *Does the chimpanzee have a theory of mind?* It was just a very exciting paper which really discussed for the first time, what's now known as theory of mind, that is, the ability to attribute beliefs or thoughts or feelings to other agents, and the ability to deceive others. So Premack's experiments with chimpanzees were about understanding of deception in particular, and he showed that in fact these otherwise very clever animals who could be trained to understand lots of things, actually did *not* understand this kind of intention to deceive. And it seemed to me that that was very, very intriguing because there were anecdotal stories about how autistic children never lied, or

couldn't understand that other people were lying. So there were some ideas like that around, but I must say I hadn't formulated them at all until we were discussing in John Morton's newly founded MRC Cognitive Development Unit, where people like Alan Leslie and Simon Baron-Cohen were new in the field, and were actually starting to be interested in autism. And I would mention, for example, that there were these difficulties in communication and there were these difficulties in the ordinary play that we saw in these children. It wasn't like the normal social role-play, the pretend play. And these kinds of ideas fitted like hand in glove with ideas that Alan Leslie brought about normal development because for him, it was an extremely puzzling phenomenon how normal children at the age of eighteen months or so, where they really have to learn about objects in the environment, what they are for, what they really are like, how they could be used, when at that same time, they were actually playfully using objects in a way that they weren't actually meant for. So his famous example is about the eighteen-month-old understanding and laughing when the mother picks up a banana and puts the banana to her ear and speaks into it as if into a telephone. Now, for Alan Leslie, it was an extraordinary question as to why the child, from then on, didn't start eating telephones or using bananas as telephones. No, the child laughed. The child knew that this was a make-believe situation. In other words, looking at an object as decoupled from its real use in the world, and this idea of decoupling was an essential contribution by Alan Leslie to the development of the theory that there was a difficulty in autism to attribute mental states to other people.

When we were all a bit uncertain what would be best to do, there appeared in the journal *Cognition* a paper by Hans Wimmer and Joseph Perner, which used and introduced for the first time, the famous false-belief paradigm, which Wimmer and Perner called the Maxi and the Chocolate Story, and which we slightly transformed into the Sally-Ann experiment, which Simon first used with autistic children. And I can show you the dolls that we used at the time.

So, here is Sally and here is Ann. And Sally has a basket, and she has a marble. She puts the marble in her basket and covers it with a cloth. Ann has a box. Now Sally wants to play outside and she goes out for a walk, completely removed from the scene. Now while Sally is out, she takes the marble from Sally's basket and she puts it into her own box, naughty Ann. Now you can imagine at this point, many four-year-olds that we tested would laugh and giggle and they would immediately anticipate what would happen next but not so the autistic children that were tested by Simon Baron-Cohen. So he would now say, "Okay, its time for Sally to come back from her walk". And she comes back and she wants to play with her marble. And he says to the child, "Where will Sally look for her marble?" And autistic children very often gave the answer, "Here in the box" – either by pointing or by saying – because of

course that's where the marble really was. But, that was the wrong answer, as you know, because Sally couldn't know that the marble has been transferred. Sally had a false belief. So autistic children who had a mental age of six, seven, eight, nine years, and were perfectly capable of understanding the little story, and could remember what happened first, and remember what happened second, could *not* predict where Sally would look on the basis of her belief.

It was one of those exciting, novel findings that, once they were known, everybody accepted them as very plausible. Now, one very important point I must make here is just having such a finding is also not enough, because you want to know how does it relate to the inability to communicate in autism, how exactly does it explain what is wrong, what is, what is sensed as difficult with autistic children. And we really needed to get to the everyday life, everyday life behaviour, and see how a lack of theory of mind, inability to understand that other people have mental states that are different from one's own; how they could explain anything at all. And maybe I should tell you an anecdote here: very early on, when we talked about this work at conferences, at parents' association meetings, one parent wrote to me very early on and said, "This explanation has made sense of one particular type of behaviour that I've observed in my son". This was a boy who could not speak at all but the parents had taught him to point towards, high up to a high cupboard, where they kept sweets for him. And if he pointed he could then obtain a sweet. And his father had observed that the son would sometimes do this even when there was no one in the room to observe him. And as a result actually, this boy was extremely frustrated and had tantrums that nobody could explain. Now the father said, "It makes sense. He imagines that everyone else knows what I know." He cannot conceive of the different mental states, different kinds of knowledge that other people have, and therefore he would get very frustrated when other people suddenly didn't give him a sweet when they had previously taught him that that was what would happen.

Autism – Sabotage and Deception experiment

The mind blindness theory, as it was called by Simon Baron-Cohen and myself, also made some sense of the observation that autistic children had such difficulty with pretence, with the make-believe play as children. And it made sense of the anecdotal reports that we know of that they did not tell any lies, nor did they understand any lying. And in fact there was an experiment that I carried out with Beate Sodian. So here you have a 'goody' and a 'baddy', and a box, which has sweeties in, can have sweeties in, and a padlock and a key, for the sabotage condition. Let me show you how the sabotage condition went. So we explain to the child that this was a game where they had to put a sweetie into a box and there were these two characters, one was a friend, and if he came and saw a sweetie in the box, he would put

another one into it, and the child could take it home. And here was a horrible thief. If he would see a sweetie in the box, he would take it away and the child would get nothing. So this was the set-up and in the sabotage condition very obviously there was a key and a padlock there, which the child could use in order to prevent the thief from getting at the sweet. So the child did this very well: the autistic child, the normal child, there was no problem. They understood what this whole thing was about but the other condition was exactly the same except the padlock and key were taken away, so this time you had no way of preventing the thief from getting at the box by any physical means. You had to use the power of the mind, power of persuasion and indeed lies. So this was how we did it. So the child has to remember to keep the sweet safe from the baddy, from the thief. And when the thief, when it was the thief's turn to ask the question, he would say, "I wonder whether this box is open or locked. I'm not going to bother to come all the long way if this box is locked". So he would ask the child, "Is this box open or is it locked?" And we were willing the child to say, "It is locked", even though there was no padlock there at all. And this is what indeed the normal four or five year olds said with gusto, and the thief would say, "Alright, I'm not going to bother". We would praise the child for having done so well and for getting the sweet. Of course, conversely, when the friend came, they shouldn't lie because the friend would put another sweet in. So we had very differential behaviour to the two, and we found that in this condition, the autistic children were unable to lie. They were very, very upset that they could not prevent the thief from getting at the box. This time, they had not physical means to do this, and they were completely lost.

So the theory of mind deficit hypothesis is an example of a very successful hypothesis that really could explain quite a lot of the problems that autistic children have with communication and social interaction. But, of course, it did not explain the non-social features of autism. And these non-social features include superior abilities, so a deficit theory is useless in this case.

Autism – detail-focus / 'weak central coherence'

We want to explain how come that there are islets of ability -- wonderful rote memory; a great ability sometimes in doing jigsaw puzzles. One of the very earliest experiments I ever did was actually comparing the ability to do a jigsaw puzzle upside down, without looking at the picture on it, and doing the jigsaw puzzle in the conventional way and it turned out that autistic children were just as good upside down as right way up. So it already gave a hint that perhaps they weren't so strongly influenced by the overall picture on the jigsaw puzzle: they could just go from edge to edge in a very interesting, detail-focussed style. And I've become very interested in these detail-focussed styles, not only in visual perception but also in the way that they use language. For example, their ability to remember isolated single words as

opposed to meaningful sentences, and thought of this as a particular way of processing information in piece-meal style; a style of information processing that gives more weight to local detail than to the overall meaning, or the overall gestalt. Now it seemed to me from work that psychologists had done in the thirties, the gestalt psychologists in particular, that in most people there is a tendency to go for the gist; to go for the overall meaning and lose the detail if need be. So, if you have to tell a story that you heard, you will give me the overall gist, I imagine, but an autistic child may be able to give me the *verbatim* story and if I then ask something odd about the meaning, may not have any way of answering me about that. So this is the kind of work that is described by the term 'weak central coherence' as opposed to 'strong central coherence', which would be going for the gist, going for the meaning. So weak central coherence denotes really the attention to detail and perhaps this has advantages, in some cases, where it's necessary to get the detail processed very well.

So this is the work of Gilles Trehin, who is an extraordinary draughtsman. He was diagnosed as autistic as a child, and I have known him from childhood. Gilles has built up this imaginary city of Urville, of which you see here some of many hundreds of pictures, which he draws in minute detail. It's growing forever in his different drawings.

There are many interestingly, many autobiographies available of very, very talented, very able people with mild autism or Asperger's syndrome, who write about their experiences, and a recurrent theme is the capture by the detail and the perhaps inability to make sense and meaning, draw it out of the whole picture. And it was Francesca Happé who really developed this theory towards thinking of it as a style of information processing that is, in fact, present in the whole population, is nothing abnormal about it, either the weak or the strong part of it; you find a normal distribution in this and you would possibly -- that's what she predicted -- find more of the weak central coherent style in relatives, in the parents of the children with autism. And indeed, we tested this in an experiment and found this to be the case, so that this style, which could be captured in certain tests, was more frequently seen in fathers of autistic children than in fathers of dyslexic children, or in fathers of a sample of control children.

Autism – a single disorder or a disorder spectrum?

The idea of the spectrum has widened the categories and of course is one of the major reasons why there are now so many more cases diagnosed of autistic disorder. So we have a huge increase, and it's of course very difficult to know whether this a real increase in the incidence of cases or whether it is merely due to this wider, wider categorisation and a greater awareness of such cases. At the moment we cannot tell which it is. But this, while it

has brought many very problematic children into the limelight and has given them also the possibility of being studied and being helped through special education, it has also had some very undesirable consequences because in some sense, the whole idea of this spectrum has now resulted in autism being a really heterogeneous category. So it's very difficult to see what the common denominator really is and whether there *is* a common denominator. In fact, it looks as if it is absolutely essential to talk about subgroups here, before we can actually get at a genetic basis. So at the moment, in my view, it is actually quite hopeless to try and find a genetic basis of everything that is in this autism spectrum. On the contrary, I would advocate that we need to go for specific symptoms, for example, weak central coherence, which is a style which can be found not just in at least a subgroup of those who are on the autism spectrum, but also in their parents. Now this could be something that has a genetic basis.

Historically speaking, Asperger's syndrome has come more and more into the focus of attention. More and more people are diagnosed with Asperger's Syndrome as opposed to autism. And the reason for this is because we can now recognise even mild variations of social and communicative incompetence/inability in people who before that would not have been considered to be in any way abnormal, but maybe considered eccentric or just very socially uninterested. So, Asperger's syndrome is at the moment quite a controversial diagnosis. While there seems to be a desire to keep it within the spectrum of autistic disorders and put it perhaps at the mild end of these, of this spectrum, with slightly less severe deficits and perhaps better abilities of compensation, better intellectual abilities which of course help the compensation, there is also a possibility that in the end it might have been taken out and put into a special category. Trying to find out whether it also has different biological origins, different genetic origins, is of course yet another matter.

Brain Substrates – visualising cognitive brain function, the brain's mentalising system

There was this very, very seductive possibility that we could move from the idea of specific cognitive deficits to underlying neurological systems. A kind of one-to-one mapping saying, "If we have identified a deficit in, for example, mentalising – the ability to attribute desires, feelings, thoughts to others – we should find a structure in the brain that deals with this". So this was a very radical idea and I think I've come to the idea quite late in my life because it seemed well, we should feel quite satisfied with talking about the cognitive level and explaining behaviour by cognitive causes. But, there were all these wonderful new techniques being developed, and of course my husband, Chris Frith, was one of the pioneers in the application of brain imaging methods to brain function, to, in fact, cognitive abilities. So it was a beginning of a collaboration, actually quite late in our life. So the first study was made possible because Francesca Happé had developed a very nice set of stories that

contrast mentalising and non-mentalising abilities. So they are called theory of mind stories, and they are called physical stories.

So this mentalising system was also revealed when we used silent animations that evoke, almost compel, attribution of mental states, compared again to silent animations that just show randomly moving shapes. So what you see here are a large triangle and a small triangle happily playing in a house. The large triangle goes out and clearly wants the little one to follow him outside, slightly nudges him to go outside and even blocks the door. Now the little one is exploring the outside and here they are happily playing in the garden. We feel this compulsion to attribute desires and intentions to the little triangles, completely unconsciously, completely automatically. We don't do anything, it's just happening. And in the other type of animation, while the triangles are just floating and drifting around and we couldn't care less. So we use the difference between these two in order to find the activity in the brain that is there when we are doing this involuntary, automatic attribution of desires and intentions.

I'm sure that there are lots and lots of components in the brain that are involved but the ones, the major ones that appear again and again, are the medial prefrontal cortex, very, very much in the middle of the brain, right near the front; the superior temporal sulcus, very much at the back. And very often, what's called temporal poles or amygdaloid region. But there are other regions. I just want to mention these as those that are particularly robust and they each have something to contribute.

One very interesting idea is that the superior temporal sulcus, which always comes up very clear and loud in all the studies about mentalising, is that it is in an area very sensitive to animate movement, and to eye gaze and to faces. It's something to do with our instant detection of stimuli as biological agents, as important things. But you see we are so driven by this that we would even think about little triangles that, after all, not at all like creatures, like human beings and little-known animals, and make no noise and have no facial expression. Even if they move in certain patterns we will also treat them as potential agents and this is particularly when this area of the brain is active.

Now, when we talk about the amygdaloid region and the temporal poles, we know that these are regions that will have to do with scripts, social scripts, to bring meaning to things so these are very important for comprehending whole stories and for giving also some emotional meaning to what we perceive.

And when we talk about the medial prefrontal cortex, we come to something that's at the heart of what's now called social cognitive neuroscience because that's an area that's active whenever we think about people; imagine people; think about ourselves. And it's particularly active when we, when we reflect, when we are conscious, when we are aware of what we are doing. Now this is what you find in healthy volunteers.

Brain substrates – visualising the autistic brain

What do you find when you scan people with autism? And I should mention here that we only scanned so far adults with autism, adults with a very mild form of autism, with Asperger's Syndrome, or what's called high-function autism, people who could consent to the procedure; and people who had actually learned everything about attributing mental states. They had the language of theory of mind and yet we knew of course they didn't have the kind of fluent understanding of mental states that we have because it was always a very hard calculation for them to answer questions about mental states, and just occasionally there were telltale errors. So these people were in the scanner; they saw and read the same stories; they were the ones who looked at these animations or at visual pictures. And what we found was reduced activation in these components of the mentalising system but more importantly, we also found weak connectivity between the components, and in particular we found weak connectivity between what we might call the bottom-up components of the system and the top-down components of the system. So here is a theme that has become familiar because we believe that if we think more about possible missed connections between top-down fibres, neurons, and bottom-up driving neurons that bring perception from the outside world inside. If we think more about that we might get at a unifying theory of what is different in the autistic brain. Why it is that they can attend to detail so much? Why it is that they are captured by all sorts of stimuli and they do not give automatic preference to social stimuli? It's the top-down processes that need to modulate our perception to give importance to certain things and not to others.

Well, at the moment, we can't be too ambitious. We have to be proceeding relatively slowly but I think the idea that we can at least talk about a behavioural level, separate from a cognitive level, separate from a brain level, and that again separate from a genetic level, helps us organise our facts and helps us tie things together in a way so that we can say, "Okay, this particular behaviour, for example, communicating non-verbally with somebody, is governed by something in the mind, by some representation of our relationship, for example, to another person. In a very abstract way, very gross way at the moment, and this particular ability can be linked using very stringent experiments in the scanner to activity in certain vast regions of the brain. So we really can't nail them down very well; we can't exactly say

anything about the content of these thoughts or of these communicative activities but we can begin, at least, to cut nature at the joints.

We really need to know much more what the different brain areas are doing, what is at the biological basis of our ability to be social, interactive human beings and this is of course the amazing important contribution that the study of autism is making to the understanding of ourselves as human beings, as social creatures.

I have never, never, ever lost my fascination for autism because every time I meet a new individual, a new child or an adult, or I talk to parents, every time I am thrown back that I know nothing; I know nothing about it. I have studied it so long and I would like to find out more so I have never ever lost this strong fascination and obsession, you could say, to find out more. It seems that there is such a paradox that absolutely forces you to think about how to solve it.

© The Trustees of the Wellcome Trust and the Wellcome Trust Centre for the History of Medicine at UCL, 2008