THE PSYCHOPHARMACOLOGY OF INDIVIDUAL DIFFERENCES
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In your 1970 book Drugs and Human Behaviour, you said that psychopharmacology is a meeting ground. One of the people who came to meet there in the early days was Hans Eysenck. Can I ask you about your view of Eysenck's work and theory?

I came across Eysenck first when I was an undergraduate because I did psychology at University College London and he taught personality theory there. That was from 1950 to 1953. I was impressed by him. He was one of the few people, who you could say gave a really systematic set of lectures on this subject. I was really impressed by what he was saying - that there were ways of approaching personality scientifically. To be honest I can't remember whether the drug part of it was in the theory at that stage but the point was that drug postulate was intrinsic to the theory in a sense ....

That was the McDougal idea, the idea that there was a factor X corresponding to introversion and extraversion ....

Well it was really the idea that there were biological bases to personality and the fact that you can examine that in 2 ways. You could simply select people who were introverted and extraverted and see whether they differed on some major biological measure, factor X or whatever it was. Or you could use drugs which shifted people along the introversion-extraversion dimension and see whether you could make people, as it were, more or less introverted or extraverted on these biological measures. That wasn't exactly part of Eysenck's published theory in 1950. The drug postulate actually came out rather later, so he probably wasn't talking at least in print about it at that time. But from the very beginning, at any rate as far as I'm concerned, there was a natural connection between what you could do with shifting people's behaviour temporarily with drugs and the sort of permanent differences in their behaviour that related to personality. So that was really how I got into Eysenck's theory as an undergraduate and then, after a while, I went to work for him.

The idea that a psychologist should work with drugs has recently been an almost alien one; were things very different then or was this just Eysenck?

I don't remember there being any problem about that. One had very relaxed relationships with medical people who necessarily had to oversee the work. I never had any problem with that. I suppose Eysenck was a fairly influential figure research wise and was able to recruit medics to facilitate the research - so it was a slightly protected environment in that respect and I'm not sure what it was like outside to be honest. One was all rather caught up within this "Eysenckian industry", as it were and didn't pay too much attention to what was going on outside! I suppose this kind of research was a slightly unusual thing for a psychologist to do, but it just flowed naturally from the kind of approach Eysenck had to individual differences (Eysenck 1963).

Looking from here, one of the key things that happened during the 50's which appeared to give the drug postulate a kick-start was the work by Charles Shagass on the sedation threshold. What impact did that seem to have then ..?

It had a great effect on me and I took some credit I suppose for doing quite a lot of work on it for Eysenck and developing that particular theme within his department. The other thing that came out of the sedation threshold of course was the link to an experimental psychopathology of abnormal behaviour. It brought home the point that a lot of individual differences in drug response, as they relate to normal personality, were just part of a bigger theory about relating individual differences to abnormal states. This was the connection to psychiatric disorder, which is fundamental to Eysenck's theory. Any work which went on that was connected, say, to drug response of psychiatric patients was automatically relevant to work on individual differences in normal personality - and vice versa. So the sedation threshold work, which was very much an attempt to find a diagnostic test for psychiatric illness also had a relevance to what Eysenck was trying to say about normal individual differences.

I got involved in that because my role in Eysenck's department was to look at the psychiatric end of things. I was attached to the Army hospital in Southampton most of the time that I worked for Eysenck and so I got interested in the psychiatric side. That led me to look at Shagass' work, which Eysenck drew my attention to, and I developed an alternative way of measuring the sedation threshold with Reg Herrington. Working in isolation in this army hospital without very much knowledge of the literature, we decided that there ought to be another way to do it instead of using the EEG. So we developed this very simple technique of getting people to double numbers while they had injections of sodium amytal. We often said afterwards that if we had read the literature on the sedation threshold we would never have done it because when we looked at it later the methodological problems were immense. Nevertheless we just steamed on and decided to do it and in actual fact it worked quite well (Claridge and Herrington 1960 and 1963; Herrington and Claridge 1965).

You were working with Eysenck from when?

Well I did my PhD in what in those days was called mental deficiency, then called mental handicap and is now called learning disability. I did that with Neil O'Connor on a quite different topic although I did actually apply some of Eysenck's ideas to temperamental differences among the learning disabled. I then, after a short time working as a clinical psychologist, went to the army hospital at Netley, associated with Eysenck's department. This was between 1957 and 1961.

When you say 'within the Eysenck group' as it were, who were the key people in the group.?

Well almost all the people who were working on the individual differences side of things, at some point dabbled with drugs. There were people like Irene Martin for example who has just retired and Harry Holland who sadly died. There were also studies by Treadwell and

Rodnight on another sedation threshold procedure, using nitrous oxide. Most of the people who actually worked for Eysenck at some point were pushed towards having a look at the effect of drugs. You must remember that I was actually in an outpost in Southampton, so a lot of people who went through briefly I didn't know.

Individual differences as construed by Eysenck - what are they for a jobbing psychopharmacologist.

Basically what Eysenck believed, and still does, was that you have a number of personality dimensions, the central one of which is introversion-extraversion, and people range along these dimensions, which are mostly genetically controlled and hence reflect different sorts of nervous systems. In the case of introversion-extraversion, he used the concept of arousal to articulate that - that introverted people have rather arousable nervous systems and extraverts have rather less arousable nervous systems. So its a kind of temperamental theory of personality. The other dimension, neuroticism, which is seen as a sort of amplification factor - if you're neurotic and introverted you're very aroused. And then the P-dimension - psychoticism is a very recent addition, which in my view Eysenck hasn't really said anything very useful about in terms of biology. But that's the basic theory.

He tied to the introvert/extrovert dimension to the reticular activating system and the neurotic one to ANS reactivity didn't he?

Well to limbic system arousal - or "activation" as he called it. He distinguished between these two ideas: arousal connected to introversion and activation to neuroticism.

What about the P axis? Nobody seems very happy with it, on the other hand it does seem to have a certain empirical validity.

Well, in so far as it refers to another domain of psychiatric disorder and the one that's sort of left over from the others, I suppose, one would expect some correlation with psychosis. In fact other approaches to the question have been more successful, particularly the schizotypy concept. This also has to do with differences among normal individuals but it was derived from direct observations on schizophrenia rather than as a more abstract factor developed from a personality theory, as in Eysenck's case. There are several things that are weak about Eysenck's P-dimension. For one thing psychiatric patients don't score very highly on questionnaire's measures of it. Secondly, its very unformed at a biological level. And finally insofar as a biological basis is proposed- that it has to do with aggressiveness - it seems quite inappropriate as a major theory of psychosis: I don't think anybody who knows anything about it would say that the crucial feature of , say schizophrenia, is extreme aggression. Quite to the contrary in fact.

What came out of the work for you? Can you give me a flavour of what it was like working on the sedation threshold?

Well, I did 2 sorts of experiment with drugs and personality which fitted in with Eysenck's drug postulate. The first used the 'fixed dose' method. Here you take a laboratory test which has been shown to differentiate, say, between introverts and extraverts or anxious and non-anxious patients and then, with a small dose of sedative or stimulant, try to shift the subject's performance on the test. In this way, according to the theory, you should be able to make the person temporarily introverted or extraverted, or anxious or non-anxious, by mimicking the underlying biological status of these personality factors. I did a number of experiments like this. But I didn't find that approach very interesting or very informative. I'm talking here especially about introversion-extraversion. I always felt it was a somewhat naive approach to understanding a complex personality dimension like that.

It was much more exciting with the sedation threshold, where you give a varying dose and where the amount of drug is itself the measure of the individual difference you are looking for. I think Reg Herrington and I - and incidentally he should be given a lot of credit for the work - found a very simple, usable and reliable method of measuring these drug differences. We showed some quite dramatic differences between subjects within psychiatric populations; we were able differentiate major groups of neurotic patients and apply the sedation threshold usefully in schizophrenia research. At that time it seemed to be a rather exciting development.

Why did it not catch on?

Well, of course it's a fairly drastic technique for a start. It's not an easy matter I suppose to give people sub-anaesthetic doses of barbiturates. It involves putting people to sleep at sometimes quite high doses, which raises an ethical question. From a diagnostic point of view I suppose you could argue that it doesn't add that much information. Perhaps it is interesting from a research point of view but one might ask whether psychiatrists really need to inject their patients with massive doses of barbiturates to find the kind of information about their mental state that the sedation threshold can give.

I wonder about that. It makes sense to say that we have extraverts and introverts and that they handle conflicts in different ways but one of the interesting things - for me anyway - is that for some reason for the last 20/30 years we've been reluctant to diagnose hysteria - as if we don't want to know about the extraverts and their reaction style. If we had a test that would detect our hysterics better, it might be useful.

I suppose from that point of view, yes. What is interesting to me having now moved more towards teaching undergraduates about psychological disorders is how much of the literature, in respect of the neuroses, just focuses on anxiety, reactive depression, in Eysenck's terms the more introverted, neurotic type of individuals. I raise the issues of hysteria and psychopathy in tutorials and lectures but it doesn't really ever catch on. There isn't a Zeitgeist, as it were, about it - if you talk about hysteria, people think of it as some kind of historical anachronism. But there are people of that sort of personality still around and, yes, it would have been interesting to have kept some sort of objective test

procedure for differentiating hysterical forms of neurosis. The thing is again people find it difficult to believe when I tell them this, but when I worked in the army hospital we actually had very very dramatic cases of hysteria.

We have it still ....

What I can remember about these people is that the sedation threshold procedure did put them out like a light. There was no kind of deception about it. Their sensitivity to barbiturates was amazing. In fact what was so interesting was the very large variation that you could find among psychiatric patients: some, the highly anxious neurotics and obsessive compulsive patients had massive resistance to barbiturates, and others, the hysterics and psychopaths were supersensitive. But the sedation threshold did seem to die out. Possibly because of the ethical difficulty in the end. But then a whole lot of test procedures like that died out. A lot of psychophysiological research actually didn't lead to any practical test measures in psychiatry really.

What else died out...?

Well I'm thinking of things that correlated with the sedation threshold, like galvanic skin response and some EEG measures - and a lot of other laboratory procedures, like perceptual tests, that Eysenck pioneered as measures of personality and psychiatric disorder. I think that in normal personality research it all faded out because it turned out to be much more complicated that Eysenck suggested. But I'm not sure that it the only reason in pyschiatry. One of the strong points about Eysenck's theory that I found, especially using the sedation threshold, is that it does work well in extreme psychiatric populations; like differentiating between disorders that partly represent exaggerations of underlying normal personality traits.

One or two other possibilities for why things fizzled out are that the drugs that formed the basis of the theory - the barbiturates and amphetamines - became much harder to use and secondly the fact that the antidepressants, when they came along, turned out to be sedatives rather than stimulants, at least the tricyclics did; was that a problem?

I think what happened with the emergence of the antidepressants and so on, was that there wasn't really a simple theory that could be locked on a theory like Eysenck's. It was after all a very straightforward theory dealing with classical stimulants and classical sedatives and I think antidepressants didn't quite fit it. And Eysenck's theory you must remember has never been very physiological. It was pseudo-physiological. He could handle these rather gross classes of difference but I think once other drugs came in then the theory wasn't able to accommodate them. And there weren't other people around with that kind of sweeping vision that he had to do it instead. Others worked along similar lines with drugs but it's been on a much more limited basis you see. So I think Eysenck was telling, and has continued to tell, a fairly simple story about fairly simple differences in the temperament aspects of personality. And drugs were just one part of that programme.

If you look back at the programme for the first 2 or 3 CINP meetings, Eysenck was a guest speaker, which probably seems extraordinary to biological psychiatrists now. But when he came out with his drugs and personality article in the Journal of Mental Science in 1957 he was really in a sense one of the few people at the start of the psychopharmacological era who had a cogent theory that was there to be tested. Were you aware that, quite apart from the work he was doing in the UK, that he was such a big name in psychopharmacology, was there a feeling that psychopharmacology was the emerging branch of psychology in a sense, or is that going too far?

I don't think actually Eysenck went down very well in America but he was very influential in Europe and I know that a number of German psychologists and psychiatrists and others were very taken with his work. My own interest at that time which I suppose was coloured very much by Eysenck was in those parts of psychology that were interdisciplinary. I was interested in psychosomatics, psychopharmacology, anything which connected psychology to other disciplines. My own view was that that's how science should be and I think Eysenck thought that too. Psychopharmacology would not be taken over by psychology but simply that there were shared concepts and methods. It didn't seem particularly odd to me that there should be that kind of interchange between naturally adjacent subjects and I think the fact that Eysenck was talking in these conferences was some recognition of that.

Who from the psychiatric side was working in this area. What about Malcolm Lader?

That's right. He's one of the outstanding figures when you think about it. He was very accepting of psychology and he was looking at the same sorts of things really, for example the galvanic skin response and things like that in anxiety and in response to drugs. This was very close to Eysenck but had more influence in psychiatry that Eysenck did. I suppose the reason Eysenck may have become less popular, was a general thing about him,which is that he has tended to try to put forward fairly sweeping and over-simplified statements that lost credibility. This has also contributed to his reputation as too much of an academic psychologist, such that gradually what he says seems less credible and valid to psychiatry. It would be interesting to know Malcolm Lader's views on that period. He was certainly the one who stands out as doing parallel research.

When did that particular period end?

For me it ended probably some time in my early Glasgow days - I continued to follow the literature but there wasn't very much after that. Around the time of my book Personality and Arousal in 1967, there was a sense that a lot of people who lost interest. I carried on with the sedation threshold for a while because the other off-shoot of that was an application to anaesthetics. The idea that you could titrate people's dose levels at it were, how much anaesthesia they would require for an operation.

Has anyone tried to do that on a mass screening basis?

Not that I know of although I did it on an experimental basis. I worked with an anaesthetist and we measured sedation thresholds using pre-medication. We found some correlation with personality but they were all rather complicated relationships and it never caught on. Interestingly, not all that long ago (2 or 3 years ago), somebody in the Glasgow Behavioural Science Department came to see me and they were working on that. There seemed to be a sort of residual interest in trying to index differences in anaesthetic levels, but it was more on-going anaesthesia during the operation than trying to work out tolerance levels beforehand.

There were one or two other people playing around with methods of monitoring. But I think it was then beginning to get detached from the personality aspect as far as I could see.

Where did your interest in LSD come from

Actually that goes back to when I worked for Eysenck at Netley. He sent me to Netley to specifically look at neurosis to try to develop experimental measures for differentiating dysthymics and hysterics. But I was rather naughty and got interested in schizophrenics in the end. I started to use some of the tests, I'd been using in the neurotic group, with the schizophrenics; this included the sedation threshold. And so my interests shifted more and more to the idea that you could apply the same kind of ideas to psychosis. Eysenck had already done that - so that was nothing very novel. But he hadn't published much on it and certainly nothing on the P scale at this point. Nevertheless it was in his early theories that you could map dimensional models on to the psychoses.

So I got interested in psychosis and when I went to Glasgow I had a sort of half-formed idea that you could apply to schizophrenia the drug postulate idea of shifting behaviour with an appropriate drug. And that's how I got interested in LSD. If you could show differences between schizophrenics, say, and normal people in a particular measure, like galvanic skin response, then it ought to be possible to produce a drug model of that physiological effect with, say, LSD or mescaline or whatever. That's what I did. When the drug was legal I gave LSD to normal volunteer subjects to see whether one could produce a temporary nervous system state, that was like that which I believed might be true of schizophrenics.

I had originally done a lot of work on schizophrenics looking at what I considered, and still consider, to be the crucial thing about their nervous system. Which is that they seem to be in a chaotic, 'dissociated' sort of state. some parts of brain function seem to be disconnected from other parts. At the time, I formulated this in terms of an arousal model: that schizophrenia was a dissociative brain state due to a failure of some kind of homeostatic mechanism, leading to peculiar patterns or profiles on psychophysiological measures of function.

One thing I did some work on to test this was the galvanic skin response and a perceptual test called the two-flash threshold. I found that the association between these measures in schizophrenics was very peculiar - and unique to them. So I then gave LSD to normal subjects and produced the same effect in them. I believe that that was a good model for schizophrenia, although admittedly the underlying physiology was obscure. But the thinking behind the method was identical to Eysenck's drug postulate: manipulating the nervous system with an appropriate drug to produce a state - in this case 'psychosis'- which replicated the state to be found naturally in some people.

Was there any correlation with psychoticism or anything like that?

I didn't know because the P-scale wasn't around at that time and schizotypy research hadn't properly emerged either. But, in retrospect and reading the literature since then - although there isn't a lot of it because of the problems with LSD - I think there is a good reason to believe, yes, that the reaction to LSD is coloured by the personality and had the P-scale or some equivalent been given, that would have come out; that is the LSD effects would have been greater in people high on a psychoticism scale or schizotypal traits. That was certainly my strong clinical impression in just looking at subjects and looking at the literature since then.

In a sense if you ask me when the period ended, I would have said somewhere around 1972 and your article on the schizophrenias as nervous types. What reaction did you have at that time... It was a very clear statement of a particular point of view...

Well it's interesting you should ask me that because I have more recently published a sequel to it..

Yes, I was going to pick up on that a bit later.

Well the reaction to the '72 article was actually rather favourable. It was accepted in a psychiatric journal (Claridge 1972). It was reprinted in the Annual Review of Schizophrenia. Yes, I think the psychiatric response to it was quite favourable. That was a period when people were perhaps less settled in their views about these questions. There was a sort of transition period between the Laingian period and a more biological era. I think people found it quite an interesting contribution which contrasts rather with its sequel (Claridge 1987).

Contrasts in what way?

Well one of the '87 referees, I might say was quite rude. Indeed I had a great deal of difficulty getting it published. It was rather insulting. I had to answer all these insulting comments.

What was the problem. If you were to publish your 87 article now, when the whole field of psychiatric genetics has swung toward a more dimensional approach, I think there would be a very favourable response.

So feelings have changed rapidly haven't they? I think that's probably true but I have to say that at the time the paper was published, the dimensional view was rather sneered at actually. It was seen very much as a psychology view. Schizophrenia had been pulled into a discrete medical model and there wasn't very much room for dimensional ideas. They looked too much like reversions to Laingian concepts, which was quite wrong in that what I was putting forward was a very biological concept actually. But nevertheless they were interpreted I think as rather anti-medical. But there does seem to be a shift back now and schizotypy is the flavour of the month and its beginning to take off a bit.

It's curious the way things go. There are Zeitgeists and fashions ..

Yes and they seem to move rather rapidly in a cylical manner..

Who else is working in this area. There are clearly the schizotypy people and psychobiologists like Cloninger and Van Praag who have recently been putting forward dimensional theories of personality. .

In schizophrenia research I would think of the American schizotypy people but in the area of more general personality research I would think of people like Marvin Zuckerman who produced the concept of sensation seeking. He's an obvious person. The other person in this country is Jeffrey Gray. His work has obviously been very much part of the dimensional tradition. In the case of Eysenck's original two-dimensional theory, he was important not only because he shifted the axes around but also because of his work to establish the proper biological basis for these axes. And of course he used drugs to do that (Gray 1982).

Do you want to comment on that. Are you one of the people who thinks that rotating the axes was a good idea

Well I think it actually says something about the whole style of Eysenck's theory. You see I think Eysenck's theory is more limited as theory of personality than he would claim. I think it is really a theory of temperament rather than personality. In other words I believe there are, for example, some fairly fundamental differences in reactivity, which you can see even in small babies and in animals. It is very biological therefore and undoubtedly in my view there are substantial genetic determinants to what I would call our temperaments and that Eysenck has rather elaborated too much into a theory of personality which I think is a broader term. Jeffrey Gray's theory seems to me to fit that temperament idea rather better. The concepts he rotated the axes to - anxiety and impulsiveness - seem to me to fit onto the brain rather better. Differences in fearfulness and anxiety make sense as basic temperamental differences which are going to be related to some brain system, whereas

differences in introversion and extraversion and so on don't seem to have quite the right sound about them as temperamental concepts or so I think ...

Too much top down rather than bottom up..

Yes, that's right. I think that Jeffrey's way of dealing with it is more plausible really because it not only fits the notion of these basic biological influences but it also fits the notion that these theories are more to do with temperament. They are much more limited actually than Eysenck claimed. They are not so predictive I suspect of a wide range of social behaviours but they are predictive of some rather extreme psychiatric states. It is very significant that if you take, say, people who have had chronic neurotic anxiety the theory works very well. This shows up in the sedation threshold results. It reflects some basic difference in nervous system responsivity relating to anxiety as a temperamental trait. Similarly with the psychopathic state or hysterical personality, where you're picking up on some deficiency in that respect, with theories like Eysenck's and Gray's - and hence with tests like the sedation threshold - you are not saying anything about, and shouldn't pretend you're saying anything about, the more subtle aspects and traits of personality that stem from this disposition.

There is some independence of personality from temperament?.

Yes. They - i.e. personality traits - belong more with other sorts of personality description I would say.

You mention Jeffrey Gray's work with drugs

Well I think in a way that Gray's theory was the salvation of Eysenck's theory in a biological sense in that Eysenck's own theory was sort of stuck with a rather old fashioned pseudo- physiological view of personality. His concepts were initially Pavlovian and then based on rather gross psychophysiological concepts. Whereas Jeffrey Gray attempted to get at the real brain even though it was in a rat. In so doing he rescued the theory, which was in danger of becoming a kind of phrenology I think. If you look at Eysenck's last statements about the biology of personality he split the brain into 2 bits which relate to the 2 dimensions, a very simplied view of it all.

I think in rotating the axes, Gray also made the theory more usable in terms of the sort of behaviours that flowed from dimensions of pesonality like anxiety. It always struck me as an awkward, and probably for psychiatrists not very helpful statement, to be told "Here we have a patient who is high in neuroticism and low in extraversion" as a description of an anxious neurotic. And that may be one reason why Eysenck's theory is not employed very much in the psychiatric setting. It doesn't seem to say very much whereas at least Gray's attempt to relate it more to the underlying anxiety mechanisms might I suppose say something about potential drug effects, for example.

Are you aware of people like Cloninger in the US and Van Praag in Holland who have tried to construct a 3 axis system, each of which is tied down to a particular neurotransmitter.

It's seems all a bit over simplified to me somehow. That's one thing that has led me away from these ideas. I'm not so convinced anymore that you can dimensionalise people's behaviour in these ways and say well that's that transmitter and that's another transmitter.

People seem to be going a step too far?

Yes too reductionist and too simplistic. It seems to me that if you select your evidence you can construct these schemas but there is a lot of cleaning up of the evidence in order to do this - I think that's even true of possibly Eysenck's theory itself - an attempt to arrive at just a few descriptors which map neatly onto some biological descriptors might be altogether too low- level really. It partly comes down to factor analysis and what interpretations you draw from that.

Maybe the factors in factor analyses of personality questionnaires are just artefacts and people and the brain just doesn't work this way. You can't take a factor in isolation and say that it is "due to something". Factors are statistical concepts pulled out, as it were, for the moment in order to look at what's making up the variation. I've thought about this quite a lot in the past about Eysenck's dimensions and other dimensions because they are not very dynamic. They are a kind of static cross sectional view of individual differences in a population but its not clear how these would begin to interact, as they necessarily have to, in order to describe the on-going behaviour of the person. You've got to construct other principles to do that. So that seems to me a possible serious flaw in these dimensional type theories.

I can think of similar examples closer to my own research on schizophrenia. If you consider, say, positive and negative symptoms, you can take schizophrenics and you can certainly factor out behaviours and say well there are positive symptoms and negative symptoms in schizophrenia. In fact in my view that isn't likely to be true. It's more likely to be a dynamic thing with positive and negative symptoms alternating or forming part of a dynamic process of psychotic behaviour. You arrive at these clusters or dimensions simply because you are analysing a number of measures taken at one point in time. But that doesn't actually represent the real dynamics of the state.

I'd like to ask you about the LSD research going on during the late 50's, early, middle to late 60's. Was that a good idea. Did we learn anything from it?

My own view is that it's a bit of tragedy that it stopped. There were mostly two reasons I guess. One is that it became an illegal drug and I suspect that scientists were rather relieved that they didn't have to bother with it any longer; and anyway at that time the 5HT-LSD-psychosis connection didn't seem all that convincing to make them think otherwise. And the second reason was the arrival of the amphetamine/dopamine model,

which seemed to add up to a neat uncontroversial story schizophrenia, antipsychotic drugs and so on. Incidentally, I don't think these two reasons are unconnected and that the amphetamine/dopamine model has been sustained long past its "sell-by date" by the lingering unease about drugs like LSD and their connotation as street drugs.

Which is clearly wrong.

Which is clearly wrong, but it seemed to catch on and it sort of eclipsed the LSD story. But the latter anyway was getting messy because of the street drug use and it being made illegal. Though I understand people were using it therapeutically until quite recently.

Very peripherally. It dropped out of mainstream very very quickly.

Yes, in research. I think it was a tragedy in a way and I think it will subsequently be realised that if we had continued with LSD or at least drugs of that general type, drugs which were psychotomimetic, then we would have found out more about schizophrenia than we have with amphetamines. My own view is that there was a failure even to address the question of what I would call face validity. If you went out to look for a drug which mimics a natural state it seems to me that you would look for a drug which patently did that. If you give anybody a small dose of LSD, well most people anyway, you're going to produce something which is pretty weird and psychotic in general and that's always seemed to me the mimimum requirement for choosing a drug model of psychosis. There may be other requirements obviously but the first requirement is that you have to have some kind of face of validity. This has never struck me as being the case with amphetamine. You can make people paranoid and so on with large doses of amphetamines, or even with small doses of amphetamines in highly sensitive people, but its not actually a natural psychotomimetic.

Yes that's interesting. For 30 or 40 years housewives were using amphetamines and there really wasn't a problem. They certainly weren't becoming psychotic and then all of a sudden it became a big issue and amphetamine psychosis was described and everybody became so concerned about this drug that very few people would be happy to have it nowadays. It's rather strange that this can happen isn't it?

Well I think it's an interesting example of the way thinking proceeds in science. People seize upon things to fit in with existing pre-conceptions. They selectively attend to certain kinds of evidence. It's almost a kind of delusional process, theory-building in science, and that's a good example of it - selectively fitting things together because they make a good story. In the amphetamine case, if you looked at it calmly it would never strike you that it was an obvious thing to do. It would have been more obvious to stick with a set of drugs like, mescaline, LSD and the other psychotomimetics. And there's no point in saying well it's not a very good model because schizophrenics have auditory hallucinations and with LSD there visual hallucinations, because that is not quite as true as lots of people made

out. Anyway even if it were true you're still nearer to the psychotic states than you are with amphetamines. But it disappeared.

What role do you think people like Hoffer had and the research they were doing. They were doing some studies with LSD, which between one thing and the other contributed to the idea that research was happening in this area which was unethical, that's a bit strong but ...

Well I think that just added to it and I think science does very much follow social attitudes. There was a sort of serious, I suppose biological side to the research, then there was the street use and then there was a sort of semi-scientific research in the middle. There was quite a lot of research like that on LSD, which had a sort of legitimacy I suppose, but which in the end it helped to kill LSD off. Some of it was actually quite interesting. There's a lot of stuff written about LSD and things like creativity but people who had more biological ideas didn't see the need to look at this stuff in order to understand psychosis.

It wasn't just the fact that LSD was made illegal. It was the fact that it actually did have an interesting experiential component to it, don't you think? There was a whole literature of that kind which was sort of on the borderline. Some of the therapeutic stuff, where it had been given to patients like alcoholics didn't have much basis to it. This was all tied up to psychodynamic interpretations, uncovering layers of personality and all that kind of stuff which, as you know, has always been dubious in certain areas of psychiatry.

I think it just drifted away on a sort of sea of psychedelic ecstacy in the end and.. I collected together some references recently because my undergraduates were asking about it. The research did seem to stop quite suddenly and, even when it was there, there was this funny mixture of research. It was either serious research or it was vaguely suspect in some people's eyes. It didn't fit into the neat kind of pattern of the amphetamine/ dopamine theory which psychiatry needed at that time. They needed to establish a firm, very biological view of schizophrenia.

Can I pick up on the point you make that LSD was associated with research on creativity - it was also associated with research on religious experience wasn't it and because of that I think it was inevitable that it would be seen as fringe work.

Oh yes absolutely. It seems to me that the history of psychiatry has been very much a fluctuation between an attempt at a hard scientific, genetic biological theory and this experiential thing. This is a tension that has always been there and the 60's, with Laing and so on, was very much a time when the latter really took over. And although LSD obviously did have potential for people working on it to talk about it as a biological model, it fitted too much the Laingian thing to ever survive unless somebody had come up with a real breakthrough. So, yes, I don't think psychiatrists were generally able to accept that within the climate that was emerging at that time. They needed to reject Laing and all that stuff. It's interesting what's happening now is that it seems as though we're growing up a bit and people aren't quite so polarised in that respect.

I think you're right. As you were saying earlier people like you and Malcolm Lader were quite happy working at a common interface during the early 60's. Then we have Laing and all of a sudden, as you say, a tremendous polarisation.

Well it was really a three-cornered thing wasn't it, if you include Eysenck? On the one hand, you had Eysenck and Laing both opposed to the medical view of mental illness. But in other ways of course, Eysenck and Laing were in entirely different camps. Parts of Eysenck's theory can fit in well with the medical model, the heavily biological part. Its the other parts - the dimensional view of illness - that set Eysenck in opposition to the medical establishment and which in a peculiar sort of way and that particular respect put him closer to people like Laing.

There doesn't seem to have been much of an LSD research network in the 1960's, which is interesting in its own right.

I did my research completely in isolation in Glasgow. I had a series of psychiatric colleagues in the Glasgow department and they were into to that kind of stuff. They took all of the psychotomimetic drugs and we decided to do this experiment on LSD. It was partly an attempt within, well put it this way, the Glasgow department had had Laing there and there were a number of people in it who, although overtly saying that they didn't really go along with his views, nevertheless had a sneaking interest I suspect in the kind of experiential bits of what he was talking about. So they would experiment with these drugs. It was all perfectly legitimate of course and anyway there was a feeling at that time that you needed to know how schizophrenics felt. You therefore needed to take something like LSD to find out, which I actually believe is true.
So some of my colleagues were taking these drugs because they felt they would give them insight into schizophrenia. I slotted into that quite well you see because I was interested not only taking it to find out that too but also doing an experiment on it to see whether one could replicate the "dissociation of arousal" effect that I had got with schizophrenic patients. I don't actually remember to be honest reading a great deal about.. well I read the usual stuff, but what I mean is I don't remember meeting anybody who had written for example at that time. I knew about Peter McKellar although I didn't actually know him well but I knew he was interested in LSD.

What about the Bradley and Elkes group during the 50's

Oh yes, indeed. I was very aware of that. In fact I was very much persuaded by Bradley and Key and all those people in Birmingham that LSD was a good model. Indeed I still use their papers and results in lectures here. They are classic papers. Certainly they convinced me that there were similarities between the experimental effects of LSD and what happened in schizophrenia. And there was Mednick who was writing about this - he had a learning theory of schizophrenia.

What's striking about Bradley and Key's description of LSD effects in animals in their 50's papers - if you read them out of context, what you would think you were actually reading

would be an account that schizophrenics had given of their perceptions and cognition. So that's what struck me about it.

The disappearance of LSD is a story that needs to be told.

Oh yes why it disappeared so abruptly hasn't been told. It's not just a case of a better hypothesis taking over from a worse one.

Do you think it fits in with the shift from the democrats to the republicans in the US and the general closing down..

I didn't want to say that.

No, but timewise it does fit. You wonder about these things.

A more rigid kind of attitude you mean .. you're probably right. There is a kind of openness of experience about LSD and that's lacking in certain periods. It may be reflected politically.

There are echoes in the story about mesmerism. It was associated with the French Revolution. An awful lot of people around the time who were actually signatories of the revolutionary papers and so on were mesmerists and of course once the revolution began to eat its own children then mesmerism was one thing that went. It ended up proscribed for the better part of 100 years.

Yes that's interesting.

Reading through your book on <u>Drugs and Human Behaviour</u>, one of the things that I'm struck by is that most of the principles of what you could call cognitive neuropharmacology there then. It's become a bit of a growth industry again in the last 5 years with a range of groups trying to explore the impact of drugs on cognitive function and re-discovering principles like asymmetrical transfer, but they're all there in your book - it's either marvellous that you had all of this then or disappointing that we seem to be reinventing the wheel - depending on your point of view. But that's another research programme that went into decline in a sense - the idea of looking at neuropsychology with drugs in human volunteers quite apart from using LSD.

Yes I think that's probably right. From the individual differences point of view of course that might have been because the individual differences effects within normal subjects can be quite complicated and didn't stand up - you got tired coping with all sorts of interactive effects, so I think that may have been why people stopped doing it.

But looking at some of the things you talked about in the book. You talk about the effects of chlorpromazine on continuous attention tasks. This hasn't much to do with the individual differences framework as such, has it? In this area, the funny thing is that there was work happening in the 50's and 60's and all of a sudden it stops and it's now being picked up again - so there's an interesting hiatus where you've got references from the late 80's and the 90's and from the 50' and early 60's and nothing in the 70's or early 80's.

Yes well I'm just trying to think what happened. Part of what happened might have had to do with what happened in psychology generally. Of course neuropsychologists have always been very concerned with looking at brain abnormality and all of that stuff has certainly been a strong theme. Then there's always been a strong theme in strict cognitive psychology, the work of Broadbent and Baddeley and others at the Applied Psychology Unit in Cambridge. But for some reason, they weren't particularly interested in drugs or physiological manipulations other than sleep.

Combining these two in cognitive neuropsychology, I agree, is relatively new. This is attempting to bring brain functions more specifically into cognitive psychology. Well maybe it simply is that up till now cognitive psychology has always been a bit of a black box kind of discipline. People didn't really want to talk about the brain. They'd rather draw flow diagrams between black boxes and maybe the lack of interest in drugs was because, if you don't bring them in, you don't have to address brain questions and maybe it's only since the brain has been brought into cognitive psychology that its been possible or interesting to take up this kind of work again.

That's the only reason I can think of - that it reflects to some extent the rate of development in different areas of psychology and over a period there was no place for a pharmacological dimension because the pharmacological dimensions had been largely accomodated within the individual differences framework, which faded out for other reasons.

Schizotypy is the other area - when did you begin to move from individual differences framework into schizotypy...

Well I see schizotypy as individual differences. As I said earlier, my interest in the basic ideas about schizotypy, although it wasn't actually formulated in that way, goes right back to when I worked for Eysenck in the 60's. When I talked to schizophrenics for the first time as a young researcher, it seemed to me, although people had warned me that they were on another planet, actually sometimes they seemed to be like any other people I had met.

It struck me that maybe this dimensional idea that Eysenck had could actually be applied to schizophrenics in their better phases. Of course they could be totally mad but quite a lot of the time they were perhaps like Laing had said, perhaps more interesting to talk to than the people in the officers' mess, which I think is what he said about his own stay in Netley - because he was also there. So, that's really where it started.

I got quite interested in the notion of some continuity between schizophrenia and the normal personality at that time. And then when I went to Glasgow, the LSD experiment in a sense attempted to shift some people into a temporary state with drugs. So the logic was just the same as with Eysenck's original drug postulate applied to introversion-extraversion. But then there was a sort of gap because I couldn't find any measures of the dimension itself. Of course if I'd been a little less insular I might have looked to the States because Meehl was writing quite early on about just this idea of schizotypy but I wasn't actually aware of it.

Eysenck then came along with the P-scale and so I started to use that and got quite interested in measuring psychotic traits in normal people. He then spoilt everything by changing the P-scale in a way that seemed to weaken it. By this time, I had come to Oxford and I had a young undergraduate, somebody called Reichenstein, who I will never forget because she said she wanted to do a project measuring schizophrenic traits in normal people. I hadn't told her about this - she just came along to me and said she thought schizophrenic traits could be found in normal people and that she wanted to try and work up a questionnaire to measure these. I sort of sat back in my chair - it was amazing really that she should have arrived at this on her own . So she then constructed this questionnaire, which was the basis of the schizotypy measures that we then developed here. Then of course the whole thing took off. I discovered lots of other questionnaires and other questionnaires since then have been constructed. And now there's an explosion of questionnaires.

When did you become aware of Meehl?

Well, not more than about 7 or 8 years ago. Quite recently. The schizotypy scene was a very scattered kind of thing. Last year I went to a conference in Italy which Adrian Raine and Mednick organised and it was the first time any group of people had come together to talk about schizotypy. That was really quite interesting because the work had been done in scattered little bits and nobody had really brought it together.

Having discovered the schizotypy literature and developed our own questionnaire which we thought was better the P-scale, we nevertheless adopted the Eysenckian strategy towards research. This was to describe the individual difference at a personality level and to find some sort of underlying biological measure of it.

Do you want to comment on the measures

What we really did and are still doing was to examine a number of different paradigms. For example, I got very interested at one point in the augmenting-reducing effect on EEG, described by Buchsbaum and others in the States and I used that for a while. Then I had a DPhil student - Paul Broks - who was interested in work on interhemispheric differences. He wasn't interested in schizotypy actually but I persuaded him to use our schizotypy scale. He was pessimistic but he did an experiment with this and found differences in lateralisation in relation to schizotypy. And then I had another DPhil student who I tried to

push in the same direction but he wouldn't be pushed. But Steve Tipper was in the Department at that time, the negative priming man who you know well. It seemed to us that the cognitive effects you get in negative priming experiments were a natural kind of description of some of things that go wrong in schizophrenics - a failure of cognitive inhibition. So we looked at it in schizotypy.

That kind of model then goes all the way back to your interest in selective attention from the 50's.

Oh yes, absolutely. The only new thing about it really was the hemispherae perspective, which was not very represented, if at all in the 60's scene. Anyway we looked at various aspects of schizotypy, including a study of relatives of schizophrenics and drug manipulations. For example, Tony Beech and I looked at the effects of chlorpromazine on negative priming, which shows that chlorpromazine strengthens negative priming. In other words it had an effect consistent with the findings in schizophrenia and schizotypy of a weakening of negative priming. So as a strategy, that in a sense goes right back to the Eysenckian drug postulate applied to an individual differences problem. I think that there is something to be learned from using this kind of two-pronged approach - too much research is isolated. I always remember a colleague of mine, Peter Broadhurst at the Maudsley hospital in London who was a Professor of Psychology in Birmingham for many years. He was a behaviour geneticist and his view was that whenever you did an experiment on individual differences, say measuring negative priming, you ought always to do it on twins because you can then answer two questions at once. You can answer the question does negative priming in this case relate to schizotypy and you can also answer a question about the genetic component in the individual difference you are studying. I have always remembered that because it seems to me that that's another example of where you can efficiently join together research approaches on the same topic.

Can I raise the question of behavioural genetics - your mentioning in it prompted in me the reaction that psychologists are supposed to be liberals who are all for nurture and geneticists are all conservatives who are all for nature etc etc but it is a case of trying to bridge that divide isn't it - the most productive opportunities lie there

I think that's right. I did once do a twin study on the sedation threshold with that sort of thing in mind, trying to see whether there was a genetic component to the sedation threshold. So I was very much into that sort of stuff in those days, trying to link all the psychos - psychogenetics, psychopharmacology, psychosomatic, anything with psyche in it I was quite interested in because it seemed to me that there's where the contribution of, or a strong contribution of psychology might lie. Not isolating itself from other areas but trying to see where it could connect up to those areas. And I was very impressed when Brian Leonard came here recently to talk about psychoimmunology, which is another example of the same thing.

Your work with LSD and the sedation threshold reminds that one of the interesting things about psychopharmacology for me is that it's one of those sciences which is not theory driven. There's always been new compounds coming out which don't fit into the theoretical framework and you've got to reconstruct things because of them. But Eysenck's work was different in that it was one of the few things that was theory driven ..

It was highly systematic, yes, and thought out but it became slightly restricted. But there were some quite extraordinary phenomena investigated. I spent my first of few months working for Eysenck, I remember, sitting looking through a handbook of experimental psychology looking for any phenomena which could possibly show individual differences between introverts and extraverts. Because according to Eysenck's theories if you take any piece of behaviour its bound to be influenced by inhibition or excitation, which were the individual differences concepts he was playing around with at that time. So I spent a whole term just reading, picking out things like time judgement and all sorts of curious phenomena like that which were bound to show individual differences. And if you thought about it you could always find a reason which fitted into Eysenck's theories. A lot of it was like that and there were some extraordinary phenomena studied. There was a thing called Bidwell's ghost for example.

What was that

It's a phenomenon where if you present say a green stimulus, as a flash of light and then you mask it with a white stimulus you see the complementary colour; you never see the primary visual image at all. So it's really the suppression of the primary visual image and its called Bidwell's ghost. According to Eysenck, the extent to which this occurs should be correlated with extraversion and be affected by stimulants and sedatives according to the drug postulate. So he had this Japanese student doing that and somewhere in the literature in one of his books I think on drugs that came out of Eysenck's laboratory is an experiment on Bidwell's ghost. So almost any experimental laboratory phenomena was up for grabs, as long as you could make some story about it being affected by inhibition or arousal.

One of the things about working in a department of experimental psychology, a general department, that I've come across in the last 20 years here, is the lack of interest in that fact from the point of view of experimental psychology. Because the point about Eysenck's theory is that its both a theory of personality and a theory simply about individual differences. So if you look at it and say, okay, we tried to explain introvert and extravert and we were using things like Bidwell's ghost to get into the biology of that. That's one view of it. The other view is if you are an experimental psychologist and you're doing experiments on Bidwell's ghost, there are big individual differences and Eysenck would claim that this theory or that kind of theory could explain these. It's interesting how very few experimental psychologists are interested in that fact. Mostly the effort is directed only towards the phenomenon itself. Nobody really pays attention to the individual variation..

One of the interesting exceptions to that is Steve Tipper because when he was working here on negative priming, he did get interested in the individual differences side and this ties up very nicely with an area like schizophrenia research. But that isn't recognised very often. Some years ago I gave a seminar in the department here and tried to make that point but mostly people are wanting to get rid of the individual differences - they regard it as part of the error variance and a bit of a nuisance.

What about the future? ..

I think that clearly you can't turn the clock back and for ethical reasons it is quite difficult perhaps to visualise, for example, giving people LSD and measuring negative priming. But I think if there were some ways round that it would be important to take them as I'm sure that looking for animal models in schizophrenia is only one approach. Inevitably I think one has to try and look for human models. I mean we know a lot about anxiety and I think that is because we have models of anxiety in humans as much as in animals. With all due respect to Jeffrey Gray (and I think he would probably agree) you have to supplement animal work with work on humans - I think that that needs to be done with schizophrenia somehow. The obvious way is the use of some kind of psychotomimetic substances other than LSD. There may be other methods. Non-pharmacological. For example, I have had somebody working on out of body experiences in my laboratory and that may be a non-pharmacological method; and I suppose sensory deprivation is another but the thing about drugs is that you can control the situation ...

To some extent anyway

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