BEHAVIOURAL PHARMACOLOGY
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One of my criteria has been to interview people over the age of 60 which you are clearly not but with your interest in history Ian and your role in the foundation of groups like the BAP and EBPS and background in behavioural pharmacology I was keen to chase both you and Joe Brady.
Joe could provide you with an interesting, very lively perspective from the other side of the Atlantic. His coverage in several areas would approximate to mine but would perhaps tend to emphasise the tradition of radical behaviourism to a greater extent. While I have a lot of sympathy with that approach which has influenced much that I have done, I cannot claim to be a true believer in all the implications.

So how did you move into the area.
How did I get started? I developed an interest in the psychological effects of drugs during the course of my undergraduate studies for a pharmacy degree in the London School of Pharmacy (The Square). It gave an opportunity for interested people to take quite an extensive pharmacology option and to do half of their final year of studies exclusively in pharmacology. One of the areas that I liked best by then was the psychological effects of drugs. I think one reason I liked it was that there wasn't a huge amount of information to get one's head around. I also had a long-standing but entirely amateur interest in psychology since school days and I suppose if I hadn't done a pharmacy degree, I would have probably have done something in the psychological sphere and perhaps ended up looking at drugs anyway.

One of the things that struck me when you were talking a few moments ago was the relationship between psychopharmacology and behavioural pharmacology and how the meaning of these terms has changed over the years. When I began as a postgraduate student with Hannah Steinberg, in 1964, I understood psychopharmacology to mean the study of the psychological effects of drugs. Only when I browsed through your first volume of interviews did I realise that some psychiatrists apparently thought the term was restricted to the use of drugs in psychiatry. Extraordinary! As the years went by the most common meaning of the term changed very substantially, I think, to mean the study of drugs with psychological effects by all available methods ranging from the psychosocial right through the spectrum down to molecular biology. I find the notion that a boundary can be drawn at any particular point, such as between neuropharmacology and psychopharmacology, to be indefensible and unquestionably damaging to everyone involved if it had been accepted. And the study of the psychological effects did not have a single all-embracing unique term. Behavioural pharmacology has a slightly different and limiting connotation emphasising behavioural approaches to psychology. There isn't as far as I know a term that will cover the whole gamut of psychological studies as pertaining to drug action. So when one has a journal called *Behavioural Pharmacology*, it's already seen by many people as a statement of a theoretical position in favour of radical behaviourism whereas I believe it is the intention that it should in fact cover as wide a range as possible of work within the psychological domain.

So I developed this interest in psychopharmacology which was encouraged by several pharmacologists at The Square, like Michael Rand, Bill Bowman and

Geoffrey West. The tracks of my career and Mike Rand's have crossed subsequently. At that time he was a lecturer and influential in pushing me towards psychopharmacology and encouraged me to contact Hannah Steinberg. Mike worked on nicotine at that time. He had a PhD student Michael Clark (now a senior scientist at SmithKline Beecham) whose thesis was on nicotine and my first contact really with the nicotine area was serving as a subject in one of Michael Clark's experiments which was something to do with the knee-jerk reflex and the effects of nicotine thereon; as I didn't smoke, I can only suppose in retrospect that I must have been some type of control subject. Many years after that, subsequent to completion of my PhD, I got into nicotine research and eventually resumed contact with Rand and Clark. In fact, Clark and I were co-supervisors of Max Mirza, an MRC Collaborative Student who completed his studies on nicotine recently.

Around 1965, thinking back about what very roughly the state of knowledge was, as far as I can recall there were a handful of substances that were discussed as potential neurotransmitters in the brain and really there was not that much known about the central actions of even these substances. So at that time the notion of relating behavioural effects of drugs to neurotransmitter systems was really quite a distant prospect. Of course a lot of people were attempting to do so but given that one hardly knew any neurotransmitters in the brain, it seemed to me rather futile to base one's whole effort upon trying to relate some particular behavioural effects to a substance when one did not really know whether it served a useful or important purpose in the CNS at all. I think that was one of the things one of the factors that shall we say encouraged me to focus on purely behavioural studies for a long time. There were, maybe fortunately, more ambitious people who felt they could do otherwise but at that stage behavioural methods for the evaluation of drug effects were also relatively primitive - most of the techniques that are widely used now were just really getting off the ground.

Which ones?

If we think particularly about the drug dependence area, there were a handful of publications on drug self-administration by the mid 60s. It looked interesting but there were no standardised procedures. Although there was a lot of potential, there hadn't been a great deal done other than showing that the phenomenon could occur with some of the classic drugs of dependence. Drug discrimination was a mysterious phenomenon that had been demonstrated but what its practical significance or utility as an assay might be was really obscure to most of us. Studies of tolerance to behavioural effects were held back by the lack of recognition that the environmental context in which drugs were given chronically was a critical determinant of outcome - the key study of Schuster and colleagues until 1964. It was a period of exploration of a wide variety of psychological behavioural methods and approaches to find out which ones were sensitive to drugs and which could be used for demonstrating clear and substantial dose-related effects of substances, effects that were of biological and not only statistical significance. Quite a lot of time in my PhD was spent just on trying to get an effect of a drug; now if I have a PhD student who spends a year or two just trying to get an effect of the substance being studied, I worry about whether I have set unreasonable goals.

At that time I think that much of the field was really exploring possible approaches. Looking at maze learning methods, operant conditioning approaches, locomotor

activity, what we now call ethopharmacology - all of those areas existed but in a rather rudimentary form and it wasn't very clear as to how each one of them might develop.

Who were the people in the field at the time. Roger Russell, Hannah. Steinberg, Michael Chance.
They were among the most prominent people. In addition, Philip Bradley and his associates such as Brian Key had done notable work on the psychological effects of drugs in the early days in the early 60s, as well as doing the neurophysiological work for which they became best known. So they had a nucleus of inter-disciplinary research there. Philip never did give up that interest in having behavioural studies in parallel with the more cellular work that he was involved with and that lead into my move to his Unit in 1974. Chance, also of course in Birmingham, did some of the early important studies on drugs and social behaviour. It was an approach that I was never personally involved with and I suppose the main reason was the difficulty of recording in an automatic manner many of the phenomena and also because I did not really fully comprehend the theoretical structure of the approach. In the same early period, Bradshaw and Szabadi were active in Manchester, Derek Blackman in Nottingham, and of course the nucleus of the Cambridge group was forming. Trevor Robbins and I put together a partial history of the early years of psychopharmacology in Britain although it appeared only in the EBPS newsletter (Robbins and Stolerman 1990).

Can I pick up on a point there. When psychopharmacology began during the 1960s, people were in very distinct groups. There were the neurochemists, neurophysiologists, behavioural pharmacologists and then the clinical people. In recent years the trend has been toward people working on common problems and becoming neuroscientists. But what you are describing seems to me almost the opposite - a field that is splintering to some extent.
I don't believe the field is splintering. Some people seem to stir up issues by emphasizing lines between, for example, basic and clinical psychopharmacology. Such an attitude harks back to the sixties. I recall during the early days within the department of pharmacology where I studied there was a neuropharmacology group who were assaying concentrations and turnover of monoamines, but those of us who were doing behavioural research never spent any time in those laboratories. We learnt nothing of significance about the neurochemical techniques other than what came out at departmental seminars and the notion of collaborative research was something that was pretty alien to the prevailing ethos. The neuropharmacologists didn't spend much time in our laboratories. It was very separate lines of work. It was a missed opportunity although whether I do not think we were unusual in missing it. There were some real scientific difficulties too. Neurochemical work with the methods of the time, such as looking at whole brain concentration of transmitters for example, showed effects of the common psychoactive drugs at doses that were maybe ten times larger than those that produced behavioural effects. That tended to put us off from seeing that there would be a lot of scope for collaboration. Of course that changed fairly quickly. In retrospect, it seems that neurochemistry was refining some of its methodology, just as was behavioural pharmacology as we mentioned earlier, and it was not until at least the mid-nineteen seventies that the potential of interdisciplinary studies was realisable. For many years there has been a tremendous amount of encouragement to people to do inter-disciplinary

collaborations. I fully support this but I think it is also important that we don't go overboard and say that only work of an inter-disciplinary nature is necessary or desirable because then we will see fewer advances within the capabilities individual disciplines.

Can we go back to University College and how you then moved to Birmingham.

During the time I was with Hannah I was influenced to a large extent by research that was carried out in the United States in behavioural pharmacology. There seems to be a different historical line here since many feel that clinical psychopharmacology developed earlier in Europe than in the USa, but this was not true for basic behavioural pharmacology. One reason was that the size of the endeavour there was larger. Another reason was that I had become attracted towards operant conditioning as a method within behavioural pharmacology and that was something that was developing much more in the United States than it was in Britain at that time. Though it has to be noted that one of the outstanding exponents of the approach was Peter Dews who, of course, had come from England.

What can you tell me about Peter Dews?

Less than you would like! Peter had left England before I became involved in the area and I did not meet him until about 1982. He was a pharmacologist who wanted to study behavioural effects of drugs who did a certain amount of work in Cambridge and in fact gave an entertaining after-dinner lecture on all of that background at the EBPS meeting in Italy this year. Now, Peter wanted to have a way of quantifying psychological behaviour effects of drugs objectively and as they actually happened - moment by moment, perhaps rather analogous to the way that pharmacological data could be recorded with a kymograph. The available methods didn't meet those criteria. When he visited Skinner's Laboratory at Harvard, he was entranced by cumulative recorders drawing out real time records of animal behaviour and of course it emerged that this type of behaviour was sensitive to a wide variety to psychoactive drugs and various types of selectivity were demonstrable. But it is interesting to note that it was very much this criterion of sensitivity - being able to measure the effect - that seemed to have driven Peter that way rather than a particular psychological orientation or theoretical approach. His work did have an enormous impact but it was a delayed impact. His early papers appeared in the early 50s but it was really in the 60s that the impact became apparent, when activity in psychopharmacology as a whole was expanding rapidly. Anyway, somewhat to Hannah's disappointment I think, I was very interested in that. I remember Hannah very clearly telling me at one point that the concerns of operant conditioning were not what she considered psychopharmacology was all about. Obviously I disagreed to the extent that I thought it could be an extremely important part.

What did you understand her position then to be in contrast to the way you were developing.

Hannah was very good at cutting through dogma and seeing where the substitution of jargon for real ideas was taking place. I think that was part of why she was rightly critical of some of the more optimistic claims that were made on behalf of radical behaviourism in psychopharmacology, although one does have to say that similarly optimistic excessive claims were made on behalf of other approaches as well. It certainly seemed to be an era where people were saying one approach could be the

way to go rather than seeing as we do now that putting different aspects together into a three-dimensional model is much more important.

I think also that very much in our minds at that time was the view taken by some of the radical behaviourists to the effect that the expression of subjective states was something that we perhaps shouldn't be concerned with. Fewer people take that view now but at that time it was something that I think bothered a lot of people. The concept of the organism as a black box with stimuli going in and responses coming out with not very much attention to what was going on in-between either in cognitive terms or neuropharmacological terms was a major limitation to thinking. Many people derived their ideas while thinking in non-behavioural terms even if ultimately the results could be explained in a less mentalistic manner, without hypothetical intervening constructs.

That having been said when I did go off to the United States it was partly for these wonderful scientific reasons but it also seemed to be a good practical move. The BTA (Been-to-America) degree was thought to be of some value and the whole experience was very appealing. And it proved to be a very good experience. I joined Murray Jarvik's group. It was a curious group that he had built up at the Albert Einstein College of Medicine in the Bronx. He was best known for work on drug effects on learning and memory. He had the idea that one could use drugs as tools to differentiate between processes involved in different aspects and stages of learning. That doesn't sound very remarkable now but in the early 1960s it was notable. By the time I was interested in going there, which was around '69, he had quite a big programme of that sort of work. I wanted to join in but such experience was very much in demand and Murray didn't have any posts available in that area. But he did have something for work on nicotine, which was a line fo work for which he was not so widely known at that time. He had published just one or two papers and an excellent book chapter which was very influential.

So when I was offered the opportunity to go to work on nicotine I realised that I would also be able to do something on drugs, learning and memory. When I actually joined Murray's group I found that in fact nearly everybody who had arrived there to do work on nicotine had come because they really wanted to do work on learning and memory; as a result, few of them had actually done any serious work on nicotine which was then highly unfashionable as a research topic in psychopharmacology. It was not universally seen as a drug of course....

Although so many people wanted to do learning and memory work with drugs, by that time it had already become apparent that the simple notion that one could take the agents available then and dissect stages of learning and memory was not really working. Murray Jarvik's group had tested in two or three procedures in rodents and in primates a vast array of the available substances and almost none of them had any selective effects on memory. Of course any drug would disrupt the performance of the tasks but they had terrible difficulty in finding anything that had any selective effects. I think scopolamine and cannabis ingredients were about the only ones at that time and of course they were detrimental. So that program seemed to me to be nowhere near as exciting as it looked from the outside; the nicotine area was just in its early stages and beginning to open up, although whether that would actually happen was not apparent to me at the time.

It took me a while to realise that I was one of very few people who had been appointed there to work on nicotine and had actually taken the task seriously. Stan Glick had done some before and that had been very important in leading into my studies. What we did was to take the techniques that I had learnt in London with Hannah, both for animal psychopharmacology and for human research, and modified those for carrying out experiments on nicotine. Somewhat to my surprise it actually worked quite well during that first year. We did obtain publishable results and it marked the beginning of a very long and happy friendship with Murray Jarvik who acquired some confidence in these lines of work quite quickly. It took about six months I suppose before he saw me as being a worthwhile person to have there instead of another troublesome postdoc, and after that he was immensely supportive.

Who actually was he. Where did he come from ?
What I would like to record is the marvellous experience I had in Murray's group. He was full of ideas, very creative in approach, although these were often rather impractically ambitious. On the other hand, I was very cautious, not a risk-taker (and I feel I have often suffered as a result), so perhaps between the two of us we functioned as a balanced unit. I was particularly taken by the the gentle and kindly way in which Murray directed his group.

What was interesting about the background at that time was that that the pharmacology department at the Albert Einstein College of Medicine in New York was one which had been very strong in psychopharmacology and drug dependence research. Murray had developed this idea of nicotine at a time when it was extremely unfashionable and there was almost no grant support for it. The reasoning there as far as I could see - to simplify it a little bit - was the world seemed to be divided into two types of people. There were those who *knew* for certain that smoking was nothing to do with drug action and that it was something that was entirely rewarded by the various types of psychological phenomena associated with smoke, the act of smoking, the taste, the smells, the sensations, the visual things and various combinations of these and that it had nothing to do with nicotine and therefore there was no point in funding nicotine research. That was half the world. The rest of the people *knew* that as nicotine was an old drug, and indeed it was having first been discovered in the19th century, and they thought there was nothing more that needed to be found out about this substance and one should work with newer and more selective substances. That line of thinking was often extended to the conclusion that there were not any nicotine receptors in the brain anyway, so the psychopharmacology of nicotine didn't really matter anyway! So for completely conflicting, diametrically opposed reasons, there was very little to encourage anyone to work in that area.

I believe that when Murray Jarvik did obtain his first grant which was from the American Cancer Society for nicotine research it was a very controversial project for them to support. The project did eventually get off the ground and he did ultimately find some people to work on it although there weren't very many in those early days. We faced a certain amount of scorn. When I said I was going to work on nicotine, one of my colleagues in the opiate area suggested that I should not waste my time on that "rubbish"; it was not really a proper legitimate type of thing for a

psychopharmacologist to do at all. Now it looks as if the evidence that smoking is drug-taking and produces dependence will be among the most influential of outcomes from psychopharmacological research. It impacts upon the 30-40% of the population who have been smokers, upon non-smokers who finally obtained some basic rights regarding the air they breathe, and of course upon the tobacco industry.

It proved to be a very rewarding experience personally, developing into a lasting friendship with Murray and working in the group because of many people I contacted there. There can be no doubt that it was as close to an idyllic work experience as I have encountered and that applies especially to the last two years after I had moved with Murray to the University of California at Los Angeles. I was able to meet numerous psychopharmacologists in North America at a time when I knew of their work but hadn't been able to put faces to it. I think in retrospect that one of the things that surprised me most was that a lot of people whose innovative and prolific publications were known to me were post-doctoral researchers or at early stages in their careers. I had assumed that because of their notable series of publications, they would be senior people with well established groups but that wasn't so. It was also clear that they had a similar perception of the activities that we had carried out in London, particularly the work that Channi Kumar and I were involved with.

Channi Kumar, do you want to talk about the work you did with him.
The University College Group was in fact cooperative with Birkbeck College where Daphne Joyce and Arthur Summerfield were located. It was spread across psychology in Birkbeck and pharmacology and psychology in University College. There was a diverse range of activities that were to a substantial extent supported by grants from the US National Institute of Mental Health. The development of that group was greatly facilitated by that foreign support. I think at that time American National Institutes did actually have a policy of seeding research in other countries. When I ultimately came to the Institute of Psychiatry, more than 15 years later, support from the National Institute on Drug Abuse, another agency of the United States Public Health Service, played a very large role in the development of my group's activities although our core funding has always been from the British Medical Research Council.

While at University College, if we go back to that momentarily, I shared an office with Channi Kumar who was also doing a PhD at that time. We spent more time talking, instead of working, than we usually have the opportunity to do now. It proved to be beneficial because together with Hannah, we did embark on a series of studies on the oral self-administration of opiates and other drugs at a time when self-administration research was just becoming an active area. I suppose we dreadfully arrogant because we felt that with 150 or so rats, we could solve the major problems in the drug dependence area within the next 3-5 years. We certainly thought we could do a lot more than we did ultimately achieve. In the long run it was the method rather than the specific results that had the greatest impact. At the time we were actually hesitant to even publish the method as such because we thought it was not new enough - there had been some oral self-administration before. But it did mark the beginning of a collaboration and friendship with Channi that has persisted right through my career.

What's his background?

Channi did medicine and psychology before joining us. He had a very different experience from mine. It was complementary and it was very stimulating to have him there because of his formal training in medicine and psychology which I of course did not have. But what was curious was that we did not have as far as I can remember a communication problem which I have often seen in subsequent years when trying to work on projects with people who are not in my discipline - a neurochemist or maybe a molecular biologist or a neurophysiologist; they often find it very difficult to understand my language and I suppose I find it difficult to understand their language sometimes as well. So there is a communication problem. We didn't have that problem although our training was very different and so that made the collaboration much more enjoyable although I don't know whether it made it ultimately more successful.

The other influence in University College in those days was Malcolm Lader who was a Postdoctoral Fellow in the same department and I was a subject in some of his experiments too. Malcolm did provide some useful comments on the studies with morphine although we never did get him very near to a rat. Ultimately it was Malcolm and Channi who were responsible for getting me to come to the Institute of Psychiatry.

But in-between I had joined the staff of the MRC in the Neuropharmacology Unit in Birmingham - that was in 1974. It was already a unit that was at a fairly mature stage of development. I think it had been running for at least 10 years and longer if one considers the period of time before it was formally a unit but was still quite a major activity. It was an opportunity to develop behavioural research within the general framework of the unit with a very considerable degree of freedom. Although the unit had a defined programme, I was not constrained very much. I told the Director, Philip Bradley, what sort of things I thought would be appropriate if I came and he agreed and I was just starting to carry it out when the MRC initiated procedures for closing down the unit. That took several years to actually occur - I was in Birmingham until 1980 by which time MRC had awarded both me and to most of the senior staff of the unit long-term appointments stretching on beyond the agreed closure date. Therefore, much of the work that we did there, with some degree of success, was done with a unit that was formally dead in a sense. That was when I first became involved with drug discrimination and taste aversion research, methods that have played a major role in much of what I did subsequently.

What were you doing there?
Drug discrimination was one of a number of methods we tried in relation to a particular series of experiments that I was doing on cocaine. We tried various ways of examining the effects of this substance and I suppose it would be fair to say that after we ran the first two animals on drug discrimination we (Glen D'Mello and I) were seduced by the power of the technique and by what I thought was a wide range of things that could be done with it, in an efficient and economical way with interesting possible relevance to what was traditionally dangerous territory for behavioural pharmacologists. By dangerous territory I mean subjective phenomena evoked by drugs. Arguably, drug discrimination is one of the ways of getting at objective correlates of subjective states induced by substances. But it wasn't only that, it was also the precision and the reliability of the method, as I saw it then without being aware of perhaps some of the difficulties that would emerge later. Notably the difficulties of interpreting intermediate or partial generalisation effects. This made it appear very attractive. It turned out to be a sensible or a fortunate move because that method formed the basis for our proposals for nicotine research that were ultimately approved by the MRC around 1980, and led into the work that I have been doing in the Institute ever since, both with nicotine and on the discrimination of abused drug mixtures.

For the non-behavioural pharmacologist are there any implications of the drug discrimination work. Clearly, if animals can do all this, humans can too. Could the methods for working on animals be applied to humans as well and would this offer anything to the field of testing cognitive function in healthy volunteers using drug probes which has been left relatively undeveloped in recent years.
Well it is interesting that you should say that because one of the things that we have done here in recent years is to maintain a comprehensive database of drug discrimination research as a service to the field - although it began as something for our own purposes. In that database one can search for the number of publications using human subjects which I am now doing and we will see how many it actually generates. Interestingly, precisely 100 publications in human subjects on discriminative stimulus effects of drugs. So work has certainly been happening in humans as well as animals.

Is it feeding into therapy in any way or into other aspects of cognitive psychology ?
It is being utilised in several areas. It is one of many methods used in drug development for characterising the effects of novel compounds and in helping to identify compounds with unusual profiles of effect. So part of the success of the field has been its widespread use within the pharmaceutical industry as part of that process. A second area is in relation to drug dependance where, perhaps to put it in a very plain way, people who misuse or become dependent upon drugs learn about the effects of the drugs as a result of consuming them. They learn to recognise the drugs in some populations of users with more precision than one would might expect. Drug discrimination, when carried out in a formal way regardless of whether it be in animals or in humans is a way of teaching the subjects of those experiments about the effects of drugs. Then they report to us what they have learned. To the extent that the identification of particular drug effects is based upon the changes in

the internal state of the organism that they bring about, it is linked to subjective changes.

Perhaps that could be put better by saying (as others did before me) that what are described as subjective changes are learned discriminative responses using language to describe phenomena in the same way that a subject trained to discriminate drugs will typically use one type of motor response rather than another. A verbal report is using language instead of motor responses to describe internal states. I think there is a very close homology of process there although that is something which is rarely explored in a specific way because it is extremely difficult to know how to distinguish that type of interpretation from one which takes a very strict stimulus-response view and does not say anything about the intervening events.

There is another angle, which is that discriminative effects of drugs may be part of the process whereby drugs prime or induce bouts of drug-taking behaviour - there may be an important relationship to do with drug dependence which has yet to be fully elucidated.

During the Birmingham period the whole issue about the foundation of the BAP began to emerge?
This blew up almost immediately upon my arrival in Phillip Bradley's unit in 1974 where at a very early stage we had learned about the development of the psychopharmacology association or academy in Britain. For the reasons I have detailed in a letter in the Journal of Psychopharmacology (Stolerman 1995), we were not happy about the way this was occurring. The idea of an association was something that many people welcomed. Of hundreds of people who were contacted about this at the time I can only recall one person who actually said that he thought there should not be a society because there were enough societies already and there was no need for one in psychopharmacology.

Your letter outlines how the debate evolved before the RSM meeting, how you had to in a sense threaten people with the idea of a letter to Nature but having got to the RSM meeting how did you view how things went there?
Well when we had the great debate on this at the RSM which was very skilfully chaired by Max Hamilton, the issues were certainly brought out very clearly. I don't think there was much coming together of minds or that either side gave very much ground there.

On one issue that did concern you they did give ground - the issue of closed membership.
That was subsequently. The result of that meeting was that the governing body of the association, the BAP, was broadened to include a wider range of people and the membership was not restricted in the way it was originally intended but I don't think those things were actually agreed at that open meeting. The open meeting was really to let everybody air their views and for us to try to get a broader representation. We did succeed in getting a broader representation in the Council although we actually lost the vote that was taken at the meeting. It was a rather complicated affair in which amendments to the resolution that we put forward were proposed which had the effect of negating it. The amendments were voted upon first

and accepted, so by the time the meeting came round to voting upon our resolution it had already been voted out. I suppose I was rather naive with regard to the conduct of such meetings so it was a learning experience.

I thought we had lost that round but we did ultimately achieve the intended effect, although it took much longer than we had hoped. There was a lot of bad feeling that persisted for a long time which was unfortunate but in the circumstances I think that if we had not taken a very firm line nothing at all would have happened because the founding group were not really convinced by our arguments, but they were convinced by the fact that a lot of people were going to oppose it and quite likely form an alternative association. None of us would have like to have had to do that.

Why did you feel the need to go down this road because in a sense there would have been other groups open to you like the Brain Research Association.

Well a lot of people who had invested a number of years in psychopharmacology research felt that this organisation claimed to represent them because it was the only one of these groups that had psychopharmacology in its title. It was distinctly different from the Brain Research Association, which at that time in London was a very informal group that used to meet in a pub to chat and have presentations over a glass of beer. This was clearly a very good way of beginning because it became a major national organisation eventually. But it wasn't covering our ground. The BAP was clearly the one in the area and it had already the most obvious sort of name or title, it was clearly purporting to represent the whole area and the prospect of just ignoring something and then starting up an alternative organisation seemed to be less satisfactory than trying to improve the one that was already coming about. There was no doubt that the people who were setting it up had put a great deal of time and effort into it. It must have been very discouraging for them to find that a group of other people were complaining about what they were doing. But because they were not really prepared to listen to our requests, initially put forward privately, it was necessary to go through this public route. I think the fact that the change was so slow, that it took so many years for this society to become the sort of the vibrant and important organisation that it ultimately did, indicates that the initial formula was not right.

Were you aware that the clinical people involved didn't really have any associations with Oxford, Cambridge or the Maudsley - it was very much a group of clinicians from the periphery as it were.

Well, that would not have bothered me much as I was in Birmingham at the time and would not have much truck with anyone who argued it needed London or Oxbridge involved. But anyone who thinks that Oxbridge was not involved seems to have forgotten Susan Iversen and the Cambridge group and David Grahame-Smith, Richard Green and others at Oxford. I don't think the people who start a society need to come from any particular prestigious organisation or part of the country but they do need to gather the support of those who do. I think that if the individuals who were starting the society had proposed to do it in a more appropriate manner, then we wouldn't have taken those steps. The argument was very much about what was being done and which areas of the subject were being represented and where would it go in the future if it had only a very small number of members. We objected to the small number of people at the start - 150 or less - on principle because it sounded

like a club for having conferences in nice places rather than for developing the subject.

When do you think BAP became what it has since become. Is it since it moved to Cambridge in 1985?
I think it does approximate to that. I think it was the style and content of the meetings which happened to take place in Cambridge that was the determining factor. I didn't think they had to be in Cambridge for this to be a success. I think the representation of the full range of disciplines is more important. Initially BAP didn't do that. There were some clinical and some non-clinical disciplines represented but not the full range and that was a major problem. I think in practical terms if a group of people do wish to set up a major national organisation then they need to involve on their side as many of the major people in that area as they can rather than setting it up and then saying please join us.

Lets move to EBPS. Can you tell me what the reason for moving towards EBPS was around 85/86 .....
Yes its roots go back a little bit earlier than that. The reasoning was that studies of the psychological effects of drugs were seen by many of us as a valuable contribution both to pharmacology, basic and clinical, and also in psychology. There were quite a substantial number of people in Europe, indeed around the world, working in that area. We felt that we didn't have a regular meeting place for this community of scientists. It was scientists predominantly, rather than scientists and clinicians.

The existing national or international societies didn't entirely serve that group. In Britain we were almost the exception because by having the BAP we had an organisation that very largely met the requirement along with covering other areas of research as well. But on a broader international scale that wasn't really so. Furthermore, the perspective of EBPS was not limited to Europe. It was always the intention that this should be open to people from wherever they come but the major focus of its activity should be in Europe because in United States there already was a Behavioural Pharmacology Society, albeit a very different group in the nature of its activities and its style. In Europe there was a need to foster the development of the subject, partly so that younger people coming into it would have a forum to present their work and to meet other people, and partly to enhance recognition of the area as a distinctive field within psychopharmacology and to help to protect it against the inevitable competitions between different approaches to studying psychoactive drugs and the brain and behaviour.

It actually grew out of a smaller European study group. Around 1979, I and others started a European group for the study of drugs as a discriminative stimuli. That was a more specialised area - at that time there were very few groups doing it. In 1979, in Birmingham, we got nearly everyone in Europe who was doing that sort of work together in one room to found a study group and I think there were about 25 of us as far as I can remember. The study group met annually for several years but they were very small, single-session evening meetings as a satellite of some other major society, usually the European Neuroscience Association. Either we had to formalise that link or we had to expand it because it wasn't really a viable activity in its original form. There was already by that time a lot of people suggesting that it be broadened

to cover all of behavioural pharmacology or psychopharmacology or whatever. We resisted that because the prospect of founding a substantial new society was fairly horrific, but ultimately we did and thus the EBPS grew out of the European study group for drugs as stimuli. The early history of EBPS was outlined in an Editorial in Psychopharmacology (Colpaert and Stolerman 1990).

Yourself and Francis Colpaert were the prime movers.
In the beginning of the EBPS, I became a front person for taking the first formal step which was forming a steering committee but that had been discussed at some length with several people. I wrote to about a dozen people in different European countries explaining a little about the idea about a European Society asking them to join a steering committee with an intention of meeting a year later in London at the time of the IUPHAR Congress that took place in 1984. So we had a year in which to correspond and discuss ideas and then we had the steering committee meeting open by the fountains outside the Barbican and..

Because there wasn't any room in the Inn?
Well, we didn't have any money to pay for a room! More seriously, I thought that if people would agree to sit around under those rather uncomfortable circumstances and possibly get drenched with rain they must be sufficiently motivated to be the sort of people I would like to have on the steering committee. We formulated a plan for an inaugural meeting two years later. The steering committee of the society became essentially that group, with 2 or 3 more people brought in. We became the initiating group for the society and the most active people at that time I suppose in developing the plans for the meeting and the society were Francis and myself. The way it panned out was that Frances took on the main responsibility for the inaugural meeting and I worked on trying to set up the foundations of a society so that there would be something that would survive beyond that meeting, to make sure that two years later it wouldn't be necessary to start all over again.

The main thing I can remember doing in that period was writing large numbers of letters and making lots of telephone calls. It sounds rather glamorous when you talk about starting a society but in fact you are sitting there at a desk or at a word processor or on the telephone; it takes up a lot of time and it has its frustrating moments as well the exciting ones. But there were many other people who, although they were not quite so prominent in the Society then, were extremely helpful with ideas and practical advice. I can't recollect all of them but I certainly remember Georgio Bignami being extremely encouraging and helpful. Trevor Robbins played a major role in shaping up our ideas although he wasn't really free to take a leading role at that particular point but of course he did subsequently by getting the EBPS and BAP together in Cambridge for the 1992 meeting. I think one of the things that enabled me to get EBPS going successfully was the BAP experience. I wanted at all costs to avoid the same thing and so I tried to do what I could to involve as many different people and to provide enough opportunities for people to put their views forward so that even if ultimately they didn't prevail, nobody could say that they didn't have a chance to participate in the development.

Ultimately it turned out that we did have the opening meeting in 1986 and it was successful in that I think the 150 or so people participating was somewhat larger than we had originally anticipated. They expressed a great deal of satisfaction with

the format of that meeting. I think there was a certain atmosphere of excitement and of achieving something. Delegates said that here they could see a home for themselves at last. That was very rewarding for us who had spent nearly 3 years getting to that point. So it was clearly going to proceed as a society and it turned out of course in parallel with the ECNP.

Had you known that ECNP was being started...
At the particular time that we initiated EBPS we did not know that there was a proposal to form ECNP. I suppose if we had been aware of that, we would have communicated with whoever was founding the ECNP to see whether or not it was necessary for there to be two organisations. Yes, ECNP and EBPS started around the same time, largely unaware of each other's existence and with very different objectives. ECNP as I understand it was a union of a number of European national societies in the area and it was intended to bring those groups together for larger meetings and perhaps other purposes. Whereas EBPS was in an area where hardly any of the countries actually had an national society devoted exclusively to that field. Also, in EBPS basic science rather than clinical practice was to the fore; its meetings are devoted to the basic science of psychopharmacology, often with concern about and emphasis on potential applications, and the depth and coverage of the science is usually much greater. There is a lot there for everybody who is doing Behavioural Pharmacology research. It is very different in that respect and it was for that reason, and in order to have enough programme time to cover the area, the society was formed. We could for example have probably had a half-day symposium within the European Neuroscience Association meetings. We might even have been able to get a couple of sessions but that isn't enough to serve the needs of the area. We have no difficulty in filling a three-day programme with two to three parallel sessions and it would not have been possible to have that level of activity within another Society, and to have had a similar degee of control of the content.

One advantage of having the breadth of ECNP and BAP is that when it comes to obtaining funds for sponsorship of meetings there is a wider pool of resources within the pharmaceutical industry from which a claim can be made. BAP can garner support through the clinical and marketing end of companies, whereas an organisation like EBPS relies upon support from the scientific research departments who have relatively small budgets for that sort of thing.

Within a group like BAP, the basic scientists will often be seen as being somewhat concerned about the input from industry and the clinical people will be seen as quite keen to have an input from industry. But taking it further, as you said there is quite a bit of funding from industry for basic science research and within a group like EBPS a significant number of the scientists are working within the industry, so is the problem not so much the industry or the funding from industry as the disease model. It seems to me to some extent that basic scientists and particularly psychologists would often take a much more dimensional view of problems and from this perspective the disease model is the problem rather than the funding from industry per se. At the ECNP programme for Venice last year things were taken an extreme I thought and all symposia were disease oriented. When meetings are so disease-oriented, the amount of science that can come in is very limited.

I don't think that that should necessarily be so because most of these diseases are studied over such a wide range of disciplines that one can see contributions from nearly all levels with varying significance depending on the particular condition. So it can be the case that disease-oriented parts of meetings can be scientificly excellent but to have the whole meeting oriented that way is sometimes a problem because one can see major scientific developments in understanding of the nature of drug actions which may go across diseases or they may not necessarily have a very clear relevance to disease at an early stage. That takes time to come out and of course that would be lost within a programme like that of the ECNP where the application very much dominates over the science. Many contributors to your earlier volume of interviews talked about a dichotomy of disease and dimensional models but that has never seemed a major practical issue to me; it seems paradoxical that as a basic scientist I am less obsessed with such theoretical questions than many clinicians. As others said before, research is the art of the possible. It's strange that factional groupings seem to have played such a big role in the development of some societies whereas EBPS has always been a partnership between industrial and academic researchers, with a generally positive atmosphere and only occasional minor bits of tension, at least during the times I was involved and aware of the inside story.

I think that as things are at the moment ECNP has gone down the route that I have just outlined to a greater extent than any other group and its unsettling almost.
Well its unsettling in some ways. For societies that might have felt ECNP to be competition it has been helpful because many many of their members don't feel very drawn towards ECNP meetings. So although originally it was very worrying because we didn't know what direction it would go but ultimately they seem to be complementary because of the focus of the ECNP being very different. Now whether or not the ECNP is serving another constituency effectively is something I don't know.

Was there something about the early 1980s that fostered the development of European Institutions of this sort. Because AEP also began in this period.
I think people were thinking more about European societies than at any earlier stage because of the influence of the European Community. It was inevitable and it seemed to be a sensible parallel to the economic union and a possible way that organisations would become recognised as filling a role in Europe. If there is a growing closeness between European nations this should also be reflected in scientific activities. Of course there were previous organisations as well. The European Neuroscience Association began in the late 70s. The European Brain and Behaviour Society was there quite a few years before that. No doubt there were others but it tended to proliferate in the 80s and there was not a development in the science or clinical spheres across such a wide range of disciplines that would suddenly made European societies appropriate if there hadn't been a political background.

When you talk to some of the other founders of the various groups there is a sense that it was useful to pull Europe together as a counterweight to the Americans, did you have that?
We did because we felt that in order to get to meetings where we could get together with other behavioural pharmacologists, it was often necessary to go to the US.

Many of our meetings have been extremely attractive for North American behavioural pharmacologists. In fact, at times there were more US members of this European society than there were from any single European country. We did that because we wanted as good a society as could be established. I think it's fair to say we were keen to have an international society but we wanted it based in an area that would be reasonably convenient for us. If it were wholly international a substantial proportion of the meetings would have to be in North America and that would not have served the purpose we wanted. To some extent we have succeeded because the meetings all do take place in Europe but they are also more expensive than I had originally envisaged and they seem to be getting more so as time goes by. It's getting harder to raise funds for student bursaries and support and some of the younger people are getting squeezed out.

The other thing we've realised is that the US organisations are rather different from ours. The Behavioural Pharmacology Society is a rather informal group that has smaller meetings, perhaps narrower in scope, so they serve a more specialised need and don't satisfy the need that we saw. I think that behavioural pharmacology as a discipline needs a prominent society to maintain its position with all the competing areas and I believe we do a better job in that respect. A lot of the American research in behavioural pharmacology appears at the Society for Neuroscience, for example, where it is not a big player. There are very few behavioural pharmacology symposia within that society; all of the work tends to come out in posters. So I think there is something we do which the American organisations don't have and that is one reason why they come.

Where does behavioural pharmacology stand now as compared with 1965?
I suppose one could see the mid-60s and much of the 70s as a period when the discipline was finding its feet and exploring its methods. During the late 70s and 80s it would appear to have become relatively strong both in terms of academic and industrial science and increasingly integrated with other disciplines and contributing to a whole range of problem areas.

Is this because during 70s and 80s the use of animal models was very important for drug development - models like learned helplessness. The industry has signed up to the idea that we need to understand the processes involved in depression or behavioural despair but that has not been eclipsed by the molecular biological approaches..
There seems to be a cycle over periods of 10-15 years, or even longer, in which the emphasis on behavioural pharmacology in industry rises, then diminishes, and then comes up again. Because of the scientific difficulties with working with an intact complex system, there will always be a need for more elemental studies - in vitro, sub-cellular and molecular studies of various types and we have seen a time when the techniques of molecular neurobiology have advanced at a tremendous rate. This has been coupled with another factor which is the difficulty industry has had in using models of psychiatric states as a critical part of the drug development process. We all know that psychiatric states have been notably difficult to model; the fundamental features of the states are not usually known and so one has models whose validity is difficult to establish. I think a lot of the difficulty has come because inappropriate models have been utilised and conclusions have been reached which were not really

strongly supported even by the data available for the particular models used. It is also the case that some of the best models have been in drug dependence but industry has often wished to steer clear of that area.

It's pretty tough for a team of researchers in a pharmaceutical firm to produce a novel compound that works. They may have a novel idea but can't find a compound or they may find a novel compound with no obvious application, but to get the whole thing together when you don't really know what your target receptors are is extremely difficult. When they get something that looks reasonably promising on the basis of an animal model among other data, they have to push it. If a team has nothing to offer it's going to have a very poor prospect of survival. So people are inevitably pushed toward promoting, perhaps more than they would like, the best that it has been possible to find. That means the importance of certain observations in models may become rather exaggerated. When you then go to the clinic and it doesn't work, your conclusion may be that animal models don't work; often I think what it means is that if you don't use animal models in a rigorous way, or just use ones that can be set up most easily, then you will have a problem. Approaches seem to vary markedly between different firms.

I think there will always be need for the use of *in vivo* research such as behavioural pharmacology as part of the drug development process because as far as I can see we are nowhere near being able to say that a particular perturbation at the molecular level is going to produce a particular psychological effect. But to say that the behavioural analysis will itself produce for you a new compound is not realistic either; in order to identify compounds you have to know something about the receptor or enzymic target as well as the behavioural target. One without the other doesn't work. I think its regrettable that people in one area think that their approach has all the answers. Very often one sees now the same mistakes that were familiar twenty years ago. The extent of rediscovery that is going on is becoming much more apparent. I can see this particularly in the drug dependence area where there has been a large amount of activity since the 1960s. Things that were reported in the 1960s or even earlier and put aside are coming up again now at meetings but often with a different name.

Is that because some of the literature from the 1960s is not on CD-ROM?
That is a possibility since people rely very much on the computerised databases now. But for us, getting into this area in the 60s, the literature was relatively small - it didn't seem small at the time but the fact was that at that time one could read a much larger proportion of all the work that had been done in the area than one can now. I suppose we saw a limited number of papers before the 50s that met search criteria but since the 60s, there has been a huge outpouring of this work much of which is still relevant so for someone coming into the area now, instead of having to catch up with 10 years work on the psychological effects of drugs as I did, they've got to catch up on 30 years of work. Its extremely difficult for someone to do that now in an exhaustive manner and as far as I can see not all groups attempt to do so, whereas we would be given hell by our supervisors if we didn't know about one particular paper - we were supposed to have read literally everything that was relevant. I suppose this a manifestation of something that goes on in society generally - there are types of knowledge that are accessible for a certain number of years and then they are lost, sometimes for long periods of time. We really to think about how to

rectify that but its not easy to see how to resolve it. Just having more review articles written is unlikely to solve it.

How does the position of science in society look to you now compared to 30 years ago?

We are increasingly asked to justify what we have done in terms of short-term practical and economic benefits, to put forward our major achievements, often in terms that are readily understandable by non-specialists. This can be extremely difficult to do because where there are advances in health care, to trace the multiple influences that result in that particular step forward may be very difficult. Its easy to point to a drug and say that came out of a certain laboratory but none of these things ever occur in isolation. I subscribe to the "cathedral model" of research where major developments are seen as comprised of innumerable "bricks" of information, any one of which may be rather insignificant in isolation but the structure as a whole would be impossible without them. Paying for the bricks is not very glamourous and that is where part of our difficulty lies. Every piece of work that goes on is based on a large amount of previous work, which may perhaps be perceived by the individual scientist in a novel way. They see something that has been missed. But to trace all the influences, including that of the unsuccessful projects is a very complex matter. That is where our accountability is very difficult because if we say that the nine out of ten projects that didn't provide a health care advance were as valuable as the one which did because they provided pointers, Equally, in relation to many of the major findings in psychopharmacology, it is futile to try to allocate dominant roles to individual scientists or clinicians who would never have been able to function without the collective endeavour.

You don't see the discontinuity that may appear to be there later.

They are there because, when presenting something in a simplified manner later you can't tell the whole story so you say "this is what someone discovered and isn't that great". But it all does build on earlier knowledge, as those who produce the more significant findings are usually among the first to recognise. In the early 70s, the development of ligand-binding methodology began with some unsuccesful experiments which nevertheless pointed the way for others to proceed. Similarly, some of the early studies on drug self-administration and drug discrimination in the late 60s showed relatively weak effects. But those early reports of studies which were not in themselves completely successfull encouraged other members of the behavioural pharmacology community to do further experiments that ultimately were successful.

Something that intrigues me is whether the potential for developing drugs that at the receptor level act with enormous specificity will be of therapeutic benefit or is it the case that most of the conditions we will be aiming for involve multiple disturbances in parallel systems so that it may not be possible to do very much better than we have already done by means of selective targetting of drug action. Does one need to take the approach, for example, as Janssen have done with risperidone, of producing a drug with multiple actions? But if that is the case, there is no reason why the two or more desired effects have to be effects of the same substance. Using combinations of two drugs would have the advantage of enabling relative effect magnitudes to be adjusted easily. This could be way back towards polypharmacy which everybody will

no doubt laugh at. This general area is not very much addressed because it is not very clear how, with the methods and theories that we have, we could address the question of useful multiple actions. This has interested me because of our work to look at drug combinations.

You said your career has crossed with that Michael Rand again, after having been introduced to the area by him.
Yes, Michael was instrumental in encouraging me to work in psychopharmacology at University College and later encouaged my work on nicotine. He's worked in the nicotine area over the years and it would seem to be a nice outcome that we both ended up working in the same place. But in fact it is disturbing to find out that we seem to be in opposite camps. About two years ago, I gave a talk on the addictive nature of tobacco smoking only to hear Michael say in his summing up of the session that this was a ludicrous notion and he then went on to question the evidence that tobacco smoke constituents have a causative role in lung cancer and heart conditions.

That incident occurred in a scientific meeting that was in part supported by a foundation whose funds came largely through the tobacco industry. There was an influence on the programming of that meeting that was subtle but pernicious, and altered its character in a manner that quite a few of us felt was unfortunate. It certainly had not been the intention of the scientific organisers of the meeting for it to go that way. In recent times researchers in the alcohol and smoking areas have become much more aware of the difficult ethical issues associated with support from the respective industries.

The whole field of substance dependence provokes extraordinary emotions. A considerable proportion of the psychiatric profession even would write substance dependence off. This isn't a disease - its a problem of living.
This still apparently is so and I find that very puzzling. Its not something that makes sense for the psychiatric community, given a number of factors, such as the historical difficulty of the disease model for many psychiatric states and the co-morbidity between substance use and other psychiatric states which can be taken as indicating that the relationship between them is closer than traditional diagnostic categories imply.

Its parallelled by a tremendous reluctance in the past for the pharmaceutical industry to have its products associated with the treatment of dependence disorders. That is curious. Obviously its going to be a negative if a drug itself is associated with dependence but it seems to be regarded in such a negative way that even having something that would be useful for it is dangerous - it might be seen as not being in a respectable area.

Within psychiatry, substance abuse seems to take the spot that psychiatry takes within the rest of medicine.
You are absolutely right there. And within substance dependence, research on different substances have varying degrees of respectability. At one time nicotine had very low levels of respectability, whereas now among most of the drug dependence community the research is accepted, the problems are seen as shared between the

nicotine and classical areas that are mutually supporting each other. Much the same seems to apply to alcohol, at least in Britain.
One of the worrying things about psychopharmacology is the extent to which many major research groups have become involved in the dependence area. We have often said we need more research in the area but one does see more and more groups working in the field which is ultimately going to be harmful to us as a discipline. If most of our effort is seen as counteracting problems that our agents have produced we are going to have a negative image.

The industry view is one that surprised me a lot when I first encountered it. It was the view that scientifically there may not be a unique problem in working in the area but we do not know how to market these substances because we've never had any before. It is said that nobody has ever made any money before out of developing a drug for dependence disorders. Then in Britain there is the concern about health service prescriptions. All these things tend to militate against getting companies actively involved. Yet I do sense that there is a change. We can all see from the published work of various companies that there is now a much stronger interest in various aspects of dependence.

Is the fact that naltrexone and acamprosate have just hit the market for alcohol dependence going to make a difference?
If they are a big success yes. Certainly a precedent for success is going to be an important factor. I think it's a question of where the market will come from for the sale of the substances that is a little difficult. Not many users of illicit substances are going to pay for prescriptions, so how are they going to be treated? This has to be looked at carefully. In that respect one is much better off trying to treat something that is legal. There is not a problem divulging that one is a smoker. The difficulty there seems to be a matter of health services recognising that this is something that they need to treat. And I don't have a simple recipe for that because one does have to take some account of the cost implications if 30% and more of the population have to be treated with a new expensive product. One of the interesting models was the behavioural intervention devised by Higgins and his group in Vermont for cocaine which involved providing rewards for people who were free of the drugs when tested from time to time. But if there's a climate that sees the use of both legal and illegal drugs as something that individuals bring upon themselves, it becomes very difficult to justify any intervention at all.

Is seems to me that these attitudes have tended to obscure the fact that compared with research on schizophrenia and mood disorders, the basic sciences, both the biology and psychology, are much more advanced in the area of substance dependence.
We certainly have learned a lot about the effects and mechanisms of the drugs. Particularly it seems that the animal models for dependence are among the best validated in the psychopharmacological arena. Where we are still weak is why, with equivalent availability and equivalent early experience, experimenting with drugs in some individuals results in a major problem developing, in some cases a minor problem and in other cases nothing at all? Most of the laboratory work does not easily solve this because if we want to work with a model of dependence we want one in which typically every subject will become dependent, which immediately bypasses that critical question.

Well that's how I would see it which makes it more surprising the area has remained...

Outside the mainstream. Yes but I don't think that's got anything to do with the amount of information and progress in the area, it's about the perception of the area by the public and the rest of the profession. It's about application of a double standard where treatments for drug dependence are seen as failures if their effects are less than permanent, instead of recognition that it is a chronic, relapsing disorder; there is no objection if someone has to have a second course of antibiotic treatment so why should there be a problem with repeated treatments in drug abuse? It is, sadly, still to do with moralistic judgements, and a real difficulty that many have in identifying with the predicament of a drug abuser.

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