

AUDIO INTERVIEW TRANSCRIPT

## Marsden, Charles: transcript of an audio interview (19-Apr-2016)

**Interviewer:** Tilli Tansey

**Transcriber:** Debra Gee

**Editors:** Tilli Tansey, Apostolos Zarros

**Date of publication:** 29-Sep-2016

**Date and place of interview:** 19-Apr-2016; Queen Mary University of London

**Publisher:** Queen Mary University of London

**Collection:** History of Modern Biomedicine Interviews (Digital Collection)

**Reference:** e2016082

**Number of pages:** 23

**DOI:** 10.17636/01015665

**Acknowledgments:** The project management of Mr Adam Wilkinson and the technical support of Mr Alan Yabsley are gratefully acknowledged. The History of Modern Biomedicine Research Group is funded by the Wellcome Trust, which is a registered charity (no. 210183). The current interview has been funded by the Wellcome Trust Strategic Award entitled “Makers of modern biomedicine: testimonies and legacy” (2012-2017; awarded to Professor Tilli Tansey).

---

**Citation:** Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Marsden, Charles: transcript of an audio interview (19-Apr-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016082. London: Queen Mary University of London.

---

**Note:** Audio interviews are conducted following standard oral history methodology, and have received ethical approval (reference QMREC 0642). Related material has been deposited in the Wellcome Library.

© The Trustee of the Wellcome Trust, London, 2016

## Marsden, Charles: transcript of an audio interview (19-Apr-2016)\*

**Biography:** Professor Charles Marsden PhD DSc HonFBPhS (b. 1943) read zoology at the University of London before going to Southampton University where he obtained an MSc in biochemical pharmacology (1967), a PhD in invertebrate neuropharmacology (1969) and a DSc in 1986. Following his PhD, he went to the University of Bergen (Norway) for three years (1969-1972) before going to the Institute of Neurology, London, to work with Professor Gerald Curzon. In 1978 he moved to the Department of Physiology and Pharmacology at the University of Nottingham, where in 1981 he obtained a Wellcome Trust Senior Lectureship, and subsequently a Professorship in Neuropharmacology (1986). From 2002 to 2008 he was Co-Director of the Institute of Neuroscience at Nottingham. During this period he was President of the British Association of Psychopharmacology (BAP; 2000-2002) and of the Serotonin Club (2008). He was awarded the J. R. Vane Medal by the British Pharmacological Society (BPS; 2002) for his contribution to neuropharmacology. In 2012 he was made an Honorary Member of the Serotonin Club, and in 2013 was given a Life Time Achievement Award by the BAP. In 2014 he was made an Honorary Fellow of the BPS (HonFBPhS).

---

**TT:** Tilli Tansey

CM: Charles Marsden

-----

**TT:** If you wouldn't mind, Charles, could we start off really with your background? Where you came from, education, family life and how you became interested in science?

CM: I was born in 1943 in Cambridge and the reason I was born in Cambridge was because of the War [World War II]. My mother was at the LSE (London School of Economics) doing a postgraduate course in psychiatric social work and, of course, the LSE was evacuated to Cambridge. So she married my father, I think it was about the day after the War began in 1939, and my eldest brother was born in September 1940; by that time they were already in Cambridge, and I came along in 1943 and we lived in Cambridge until 1950, when we moved to Saffron Walden, which is not far from Cambridge. My father was in the army throughout the War. So I was born in Cambridge by chance, though my parents both had been to Oxford and my mother came from Lancashire, but my father's and mother's families really came from all over and on my father's side our basic origins were Derbyshire. But I have Scottish, Welsh, Northern Irish relations, so they were pretty broadly based. My father was a journalist and he was on the D-Day Landings on about Day 3, I think. He went all the way to Berlin, in fact. When he came back, he worked in the new European part of the BBC World Service and had book programmes and an early version of *'What the Papers Said'* type programme.

So he was a producer and broadcaster and he was also a writer. I was at the exhibition at the National Portrait Gallery, yesterday, of the Russia artists and we noticed that in the book based on the exhibition was

---

\* Interview conducted by Professor Tilli Tansey, for the History of Modern Biomedicine Research Group, 19 April 2016, in the School of History, Queen Mary University of London. Transcribed by Mrs Debra Gee, and edited by Professor Tilli Tansey and Dr Apostolos Zarros.

a quote from my father's book which came out in 1942, called *Palmyra of the North*, which was about the history of the birth of St Petersburg.

**TT: I have that book myself - I'm fascinated by Russian history.**

CM: Well he had spent time in Russia in the past. So I came along and my mother, as I said, was involved in psychiatric social work and worked at Fulbourn Mental Hospital in Cambridge, having graduated from the LSE. She was very lucky to graduate, actually. She'd been to Oxford and then she'd been to the Sorbonne and done various things. She was lucky to graduate because you weren't allowed to be a postgraduate if you were pregnant, and she hid that; my father was, of course, away most of the time because of the War. So she was lucky to graduate, but with the help of some friends they always concealed the fact that she was pregnant and so, she was okay and got through. And she loved her job and I used to go to Fulbourn Mental Hospital. She was a very outgoing person; sadly, she died rather young, but she used to bring patients home and they used to come and help us plant potatoes and stay the weekend, and so forth. And they used to tell us the most extraordinary stories, you know, at breakfast time, which, of course, I had no understanding of at the time. They had met extraordinary people overnight - they met the Queen on a regular basis, all those sorts of things. And of course most of them were borderline schizophrenic. And my mother also collected art that they produced and we had rugs, which we still have, and these have extraordinary scenes on them. So I think probably that was one of my earliest interests in mental health, though as I grew up I was really most interested in zoology and, of course, then they hadn't really made the connection between mental health and science, and it was still a rather grey area in my teens. We moved to Saffron Walden, went to school there, and then I went to Gordonstoun when I was 13, and I was there for four years. I got scholarships and other financial help. I got a bit bored with school and so I went to Cambridge Tech to restart my A levels; while I was at Gordonstoun I'd done English and biology and then I went to the Tech and did the three basic sciences in a year, as was customary then. The Cambridge Tech was a fantastic place, it's now, I think Anglia University, because most of the people who taught there were either related or linked to the University in some way, and they were fantastic teachers. I had a brilliant chemistry teacher and a biologist as well. And that really set me up.

And then I ended up going to London, I went to Chelsea College where a lot of fellow pharmacologists met up. There was Richard Green of course and there were others too. Mike Tyers, I think, at the same time, but there were a lot of us there. Actually, we all converged later in life. Because I did zoology, some were doing pharmacy, some were doing other things, but we all met up as pharmacologists in later life.

**TT: Can I just ask you, when you were at school in Gordonstoun, you did biology and English?**

CM: Yes, as my A levels.

**TT: Did you have a particular encouragement to do biology? You said you were already interested in zoology?**

CM: Yes, it was a very different place, I imagine, to what it is now as we're talking. I was there from 1956 to 1960, and I thoroughly enjoyed it. It really did allow one to develop one's own ideas. With a great friend of mine, we set up an apiary, so became interested in bees and we were able to get hives and bees and so on. And so it was a place that encouraged one to do what one wished to do. And we weren't strictly programmed and it was very free in that respect. I was actually very good at sport, but it wasn't obsessive about being brilliant at sport and having the best rugby team or whatever. It was very much a system that wanted people to take part and do things and explore their own interests.

**TT: You must have had a serious interest in science if you then went to Cambridge Tech to do more science A levels?**

CM: Yes, I'd already decided that's really what I wanted to do.

**TT: But you didn't do that at Gordonstoun? You just did biology?**

CM: I did biology as well as English. I supposed the English came, very much from the home side of my life. My mother wrote a novel that came out in, I think, 1953, called *Catherine Brooke*, which was about life in Cambridge during the War. It was published by Faber & Faber. But I think I was still slightly undecided at that stage. I had a background where my father was in the BBC, and when I went back to school I would always go to Bush House, because the World Service was based in Bush House. And I was always fascinated by going to the canteen with him and meeting this exotic array of people that one met in the World Service. So I was undecided, but I felt I knew what I wanted to do when I left school, and went to the Tech that I had made the decision.

**TT: How did your parents react? You come from quite an academic kind of background, not particularly scientific. Were they surprised?**

CM: I came from the background that they never really told me to do anything. They left everything open to me to decide. I'm one of four boys.

**TT: Which number are you?**

CM: I'm number two. The eldest one went to Cambridge and read history, or did he read English? No, he read history, I think, and he went into the Foreign Office. And then there was me, and the next one down, he went to Cambridge too and he read English, and went into the British Council in the end. And the youngest one did agriculture and became a farmer in Venezuela. So you know, we were all just really left to decide. We were encouraged very strongly, had a tremendous atmosphere at home in terms of stuff to read, and because of my father's position at the BBC, we had all the weeklies and newspapers and I was, and still am, an avid newspaper reader and read them all. But I was never pressurised into doing anything in that respect.

**TT: So you decide yourself, you're really interested in science, Cambridge Tech, then you go to Chelsea to read zoology. Why Chelsea and zoology?**

CM: I suppose I'd been at a boarding school and I wanted to get out of that atmosphere, or that environment. I didn't want to live in a college or anything like that, and London just seemed a great place to be. It's one of those places where you have to be at some time in your life. And Chelsea, well I had heard of the Professor at the time, Professor Purchon. He was a mollusc expert. And I just wanted to go to London, I think.

**TT: But why zoology?**

CM: Why zoology? I liked animals basically and there was another reason too. I was interested in them and how they worked, and certainly my father - though he had done history - he was also interested in animals and always, made sure, I had appropriate books to read. He got an enormous number of books to review and, in those days, what journalists did with books they reviewed, was they sold them, it was their beer money really. My father used to sell a lot though he also brought home the ones that we'd really like to have. So I had quite an interesting collection of science-related, zoology books before I ever went to university. So I think that was another factor.

**TT: But during your degree, or at some stage during your degree, you decided to continue to develop your career in science?**

CM: Yes, well one of the things I did during my undergraduate time, was to organise an expedition to the Azores with five other students. And that is when I got a real interest in science and the detail of science, because having gone to the Azores, made a collection, quite a large entomological collection; I was supported by the Natural History Museum as one of their summer scholars, to actually do all the classification work there, and then to publish the data. And that was a very interesting experience because it taught me a lot about the need to be very careful about detail, and how important it was to get information correct and to record it

correctly. And also, in planning the expedition, we had to raise all the money and get all the gear and ship stuff out to the Azores and the Natural History Museum were very, very helpful. And I went with one of my colleagues, Jim Prior, who now lives on Victoria Island in Canada, to meet the Head of one of the Departments at the Natural History Museum, which Department was it? It wasn't the Entomological Department, or was it? I think it could have been. But anyway, when we arrived he was in a deep discussion with one of his staff, who had built a model of the mouthparts of some insect or crustacean, I can't remember the details, but he had built this very elaborate model, I think, and the boss guy said, 'He's got it all wrong!' Anyway, he showed us around and he arranged for us to get a great amount of absolute alcohol to take out and store specimens in, and also arranged for the specimens to come back to the Natural History Museum.

And then, when we got back to his office it had been totally trashed by the researcher who had just gone through and thrown all the boxes everywhere and everything was all over the place. I can't remember the name of the Director of this section at the time, and maybe I shouldn't say it, but he was very calm about the mess and just said 'Oh, it happens all the time.' [Laughter]. That was mid-1960s.

**TT: So coming to the end of your degree, what were you thinking of doing?**

CM: I got a place at Durham to do ecology, because I was very keen also in travel. Whenever I got the opportunity, I would go off. That came from my background because my father and mother travelled a great deal. And the whole family travels, and this has gone on through our next generation as well, our children. So ecology seemed very relevant at the time, but also an opportunity to do things around the world.

**TT: But this would be quite an early period really for ecology?**

CM: Yes, really it was beginning to make its impact at that time. You know we're talking 1965-1966, as I graduated in 1966, so I'd begun looking in 1965. But I had also, during my zoology degree, become interested in the brain and had begun to read various books, and so forth, and I had become aware of this for mapping neuronal pathways particular technique. It was as you know well, not immunohistochemistry, but fluorescence histochemistry, which did make such an impact at that time. And I saw pictures of these tracts in the brain all lit up and so I did just almost on a whim decide, 'No, I'm not going to do ecology I'm going to do more pharmacology.' I went to Southampton and I got a place on their new biochemical pharmacology course. And the one of the Heads of the Pharmacology and Physiology Department, there were two of them, one was Professor [Gerald] Kerkut, and he was the one that I particularly knew and got on with, and I ended up staying on to do a PhD, and that was on snail brains.

**TT: And the other Head was Kenneth Munday, wasn't it?**

CM: Yes, it was. It was Ken Munday, yes of course it was. And they were quite a pair really, but they were successful and powerful at that time and had really built up that Department. I was very lucky to be there at that time, there was also Professor Akhtar, there, a biochemist who was very, very good. The people that I worked with were Robert Walker and Geoff Woodruff; Geoff who later went on to become a very important biochemical pharmacologist and a leading figure in the BPS.

**TT: So you did the MSc there? That was quite an innovation at the time, wasn't it?**

CM: Yes, I think it was the first year they had it, and I think it was Geoff Woodruff who had set it up. He was young, not much older than me, it was his first job and he'd recently got his PhD. So I did that because that seemed a way into pharmacology and really get some understanding of drugs, how they worked and what they did. I think the fluorescent mapping of the brain pathways for dopamine, 5-hydroxytryptamine [5-HT; serotonin] and noradrenaline did open up a lot of ideas about how drugs might work and so I felt it was necessary to understand the pharmacology. But, funnily, going back to my childhood, my grandfather was keeper of books at the British Museum, so for part of my father's childhood, they actually lived in the British Museum at that time. A great friend of my grandfather's was the pharmacologist, Sir Henry Dale, when my

father was Deputy Head of books living in Hampstead, and they lived next door to each other. When Sir Henry Dale was very old and he was in a nursing home in Cambridge, as a child I used to go with my father to see him. So I did meet Henry Dale as a young boy.

**TT: Do you remember much about him, because Henry Dale was a good age by then.**

CM: No I don't remember detail. I remember he was a very old man. But it's something that I remembered in my mind, because when his name came up later, I immediately think 'Oh, I remember him.'

**TT: So you do this innovative MSc and at some point you decide or are encouraged to do a PhD with Gerald Kerkut?**

CM: Yes. How did it come about? I suppose we got on quite well together, and he was an interesting character, and I did a project using fluorescence histochemistry and, obviously, I made it work. It worked. You know about it! [Laughs]. The art was to get the formaldehyde in the right condition. Gerald encouraged me, I decided I wanted to do a PhD and he encouraged me to stay on. I went for an interview at Pfizer's and was offered a job, and I said I wanted to do a PhD, so in fact they ended up providing some of the money and so it all evolved like that.

**TT: Did you have MRC [Medical Research Council] funding or SRC [Science Research Council] funding as well? Or was it all from Pfizer?**

CM: It all came from outside, I think.

**TT: Again, that was quite innovative.**

CM: Yes, I'm not exactly sure. I got a grant, but in those times, it was about £300 a year.

**TT: Was there any expectation you would go and work for Pfizer afterwards?**

CM: No, no. It was interesting. I can't remember who interviewed me there and I remember going down on a Sunday, because the interview was on a Monday, and they put me up at a hotel, and I had just completed my MSc, and I said that I was interested really in doing a PhD and they said 'That's good, that's what you should do.' And they had, you may remember, a drug called 'para-chlorophenylalanine', which inhibited 5-HT synthesis. Well, they produced that at about that time, and so some of the work that I did on the snail brains involved use of the drug, and that's how the funding and help came.

**TT: And when you finished your PhD, you then moved to Norway. How did that come about, were you interested in more comparative pharmacology?**

CM: Well it's one of these things that happens in life. I had a great Norwegian friend. As children we'd always done foreign exchanges, arranged by my mother principally, and we used to have also a lot of summer visitor. We lived in quite a large house in Saffron Walden and in the summer holidays we would have French, Greeks, all sorts of people, children, who would come and stay in our house. And we used to show them Cambridge and take them punting and all those sorts of things, and generally muck about. And I had a very successful exchange with a Norwegian family, a guy called Trond Hafting. I'm still very close friends with him and know him very well and all his children, one who is a very well-known neuroscientist now.

**TT: Who is that?**

CM: He's called Morten Hafting. He worked with, now I've forgotten the person's name, who got the Nobel Prize in Oslo about two years ago.

**TT: There were a couple of them, weren't there, husband and wife? The Mosers.**

CM: Yes, and Morten, Trond's son, or one of Trond's sons, and his wife both worked with that team, and were very much lead names on the key paper. I'd been to Norway and loved it and then just by chance a medic and pharmacologist called Hans Cato Guldberg, who was working at the MRC Brain Metabolism Unit in Edinburgh, this was 1966, he was going back to Bergen to be the Reader/Professor of Pharmacology in the Pharmacology Institute, and he wanted to set up fluorescence histochemistry, but he didn't want to hire a Swede.

**TT: [Laughs]. Almost compulsory in those days.**

CM: I shouldn't say that, but that was one of the reasons, and so he approached me as he knew the sort of work I had been doing. And so I said 'Yes.'

**TT: Because, that remark about Sweden, it was always said that you needed the dry air of Sweden to get the formaldehyde to work. I used to try and make it work in Naples in hot, humid conditions.**

CM: You had to have a good freeze drier for a start, and getting the formaldehyde right was a key part of it, wasn't it?

**TT: You had social reasons, you had family reasons, to go to Norway? To be offered a job there must have been quite astonishing, or was it not?**

CM: Yes, well it was, by this time I'd got married and we were keen to travel, in those days you normally went to America. But I was very keen on cross country skiing, another reason to be going. So it just seemed like a good idea. It wasn't possibly the best career move one could have made, but it led to three very happy years.

**TT: Did you go on a fixed-term contract? Or did you and your wife think, 'Right, let's go for three or four years.'**

CM: We went with an open mind actually. The first year was quite difficult, it always is. The Norwegians where I worked, of course, all spoke English and later my wife got a job with what was the equivalent of the Free University in Bergen and taught English, because she had read English at East Anglia. And so we both worked, but we also travelled around the country a lot and she, in particular, became really fluent in Norwegian. Mine's reasonable but hers is very good and she's very much a linguist. So we had a great time. It was there that I moved from the snail to rodents; I didn't do anything with snails there, just a little bit on my own to complete some things that I wanted to complete. But as a group we used the rat and I moved to the rat, so to speak, and became much more orientated towards the mental disease area, which is where I'd wanted to get to in the end.

**TT: Well, that really comes back to what you were saying about being a child and meeting people with mental health problems. At what point did you make the connection between what you were doing in the lab and brain chemistry and mental health?**

CM: I suppose certainly in my later years in Norway and towards the end we had a visit from Arvid Carlsson who came to see us, because I'd set up the rotating rat model, the Ungerstedt model, it had just come out in Sweden and we were able to make it work. And I'd begun to look at how that 6-hydroxydopamine model interacted with the serotonergic system, and what involvement the serotonergic system might have. We did this by doing lesions in the raphe, as we thought there might be a link between dopamine and 5-HT. When Arvid Carlsson came, he was very supportive of what we were doing and, I think, that he'd already made a major presence for himself as a dopamine expert. Years later he came to the BAP when I was the President-Elect and he gave the annual major lecture at the summer meeting, and I took him out for a meal and we were chatting about the past and interestingly he said when he looks back, how impossible his career would have been now. He published all his brilliant dopamine research in very low impact journals. He said, you

know, basically a handful of people read them and he said he could never get hold of a job now with the profile he had at that time, how much matters have changed, and whether it is for the better in terms of science is an open question.

**TT: It's probably true of most of us.**

CM: It is, yes. That's another discussion really, the whole question of what relevance the impact factor has in determining people's lives. I think it's a very poor indicator. Anyway, that's another issue.

**TT: But to just finish off your Bergen story. You went there to set up fluorescence histochemistry?**

CM: And then didn't do much. We did a bit. We got involved, that is myself, Hans Guldberg and Ole Jacob Broch, with catechol-O-methyltransferase [COMT] and trying to further identify the role of COMT. Monoamine oxidase [MAO] had obviously taken a major functional role in the amine story due to the development of MAO inhibitors as antidepressants, but there was always COMT as well, and we did quite a lot on the functional role of COMT: first in the peripheral system using salivary gland preparations, and later in the brain.

**TT: In which species?**

CM: In the rat. Ligating the salivary glands and I did the fluorescence histochemistry in those, but then we moved on and dropped the peripheral system, and moved into the brain. Hans Guldberg and I ended up writing a review for *Pharmacological Reviews* on COMT. Then came a time after three happy years when we needed to think about future plans, My wife Lucilla's father had retired and he was ill, and we were torn actually between the UK and Norway; my mother was already dead and my father wasn't very well either at that time. They were torn about coming back or going on and we were also thinking about having children, and so we did come back. There was a possibility that Hans Guldberg and I would go off to Astra in Sweden together at one time, that was one option. He then became the Dean of Medicine in Trondheim, so he moved. But that was after I'd left. But we decided to come back and I came back to Queen Square.

**TT: Well, you came back to it with Gerald Curzon?**

CM: Yes.

**TT: Did you already know Gerald?**

CM: No, I don't think I did. I'm trying to remember. I think I wrote to him. I think he'd got a programme grant, and I'm pretty sure I wrote to him to ask about positions. I don't think it was advertised as such, and I came over and he offered me a job, and then we were a bit slow about actually leaving Norway, because we were still reluctant to leave. But, anyway, in the end we did leave, and we came back to Queen Square.

**TT: And what was your project called?**

CM: Well, the project was part of the programme grant. My particular role was to look at the importance of tryptamine as opposed to 5-HT, and the interactions between tryptamine and 5-HT, which was quite interesting. It took a lot of work to get the assay going for tryptamine, and I don't think we really ever absolutely got the best one, because the techniques were not available, there was no HPLC [high performance liquid chromatography] or mass spectrometry at that time. We can come onto that side of the story later. And I am sure you know you need mass spec, really, to be able to get the really low levels of tryptamine that we now know there are in the brain. But the levels did shoot up if you gave a MAO inhibitor; they rocketed up. So the potential for producing tryptamine in the brain was certainly there. But while I was with Gerald, and having done the rotational work with the 6-hydroxydopamine lesion in Norway, my driving ambition was to look further at the relationship between dopamine or 5-HT and its influence on behaviour. How could one begin to look at that? So Gerald, who was a biochemist, and very much the

biochemist at that time, was slightly reluctant to get involved in behaviour, but he did. In the end he went along with it. I was very friendly with Michael Joseph, who now sadly is dead, but he had worked with Gerald before I was there, kept close contact, and he and I developed a close working relationship. And of course Richard Green had also been with Gerald and had done his PhD there. At that time, I think Richard had just returned from America, working with David Grahame-Smith at Oxford. The three of us had quite a good relationship and then there were Peter Knott and Pete Hudson, who were also in the lab at that time, and Barbara Sahakian came just after. There was quite a collection of people going through Gerald's lab, all who did reasonably well. So Gerald obviously fostered something. There was something special going on in Gerald's lab. Anyway, I was interested in getting behaviour going and not in a sophisticated way. It really was a pharmacological model that we could use to assess the effects of drugs at that stage. Gerald got a renewal for the grant and some point later, about a year before I left, we decided to go back to the MRC and ask for video equipment to record the behaviour. Nobody really did that in rats at that time or at least very little was done. We had a visitation by the MRC, and the guy - I won't say who it was but - was a real behavioural person from Cambridge, you can probably work out who...

**TT: Yes, that narrows it down a little, doesn't it?**

CM: ... of that generation. And he was extremely rude about us using behaviour as part of pharmacology; he just couldn't understand why pharmacologists like us would want to measure anything to do with behaviour at all and, I have to say, I think I had made a very good case, but he was incredibly rude, I thought anyway, what a nasty piece of work. That's how I felt at that time. But, actually, we had some money in the bank, so to speak, and we just went along to Tottenham Court Road and bought all the video equipment and it was a great success.

**TT: When you say recording behaviour in rats, what kind of behaviour were you doing?**

CM: Well to begin with, it was very simple or that is what we thought. This included sexual behaviour and that's where I think we came a bit unstuck with the MRC visit, because he said things like 'You know there are 59 different steps in a sexual encounter between two rats.' Yes, even far more than that. It went on and on. He was absolutely right, but in terms of trying to determine whether drugs affected sexual behaviour, we didn't need to go into that detail, and we didn't have the experience to do it. But anyway, so we did that and also measured exploratory behaviour, and so on.

**TT: That was quite a departure for Gerald's lab?**

CM: Yes, it was.

**TT: I hadn't realised that you'd obviously infected him with that, that was how he got into this behavioural stuff.**

CM: Yes, very much. He hadn't done any behaviour, and we encouraged him to do it. I invited Gerald to the dinner at the 5-HT conference in Oxford for the 'International Serotonin Club', as it was still called then, which both myself and Richard Green were involved as organisers. Gerald came to the dinner and he said he thought what a big contribution we had made to his research life, because after that he did a lot of work on rat behaviour. He also said he always felt rather bad that he'd been so difficult about letting us do it and hadn't acknowledged what a contribution that it had been.

**TT: And when is this dinner you were talking about? This is the International Serotonin Club?**

CM: We are talking now about 2008, just when I retired.

**TT: By this time in your career you've actually built up quite a repertoire of techniques and approaches, because you started off with invertebrate experience - which is unusual - and particularly when you**

started talking about brain chemistry and receptors and things like that, invertebrates are somewhat different.

CM: Yes.

**TT: You then moved into rat, and then you got fluorescence histochemistry. So you've got morphological techniques. You then are starting to think about function, the lesioned animals and what is happening, and then there's the basic pharmacology/biochemical approach, and behavioural experiments. So you've actually built up a considerable technical portfolio.**

CM: Yes, and I still hadn't got to where I wanted to be. Really what I wanted to be able to do was to measure release and tie the two (release and behaviour) together. I was lucky with my PhD in that I had a lucky break. I did find a very large dopamine cell, because you probably know in invertebrates all the dopamine cells were very small in the snail and leech, while the 5-HT ones - particularly in the snail - some very large and a lot of people did electrophysiology on snail neurons looking at the effect of drugs. What relevance that had to later pharmacology is another matter, but at that time it was an interesting approach. I was very lucky in that I stumbled across this large dopamine cell, you could see it in a whole-mount of the ganglia, and it was all because there was a student who was doing a PhD in the same lab, who wanted to measure haemoglobin in snails and snail brains.

**TT: Haemoglobin?**

CM: Yes, and there was only one, that was *Planorbis corneus* and so she got in 500 snails, and I agreed, together with somebody else, to help her to dissect them all and collect the samples in exchange for a few snails that I'd look at with the fluorescence histochemical technique. And there was this enormous dopamine cell.

**TT: These are the kinds of things one cannot write in a grant application.**

CM: No.

**TT: That's a fascinating story and it's also something about the different species and getting the right animal.**

CM: Yes, it is.

**TT: But can I come back now to Institute of Neurology and Gerald, this portfolio you've built up. You've been there for four years, four to five years?**

CM: Yes, I went there in 1972 and I left in December 1977. I was looking for a permanent job and it seemed the time to do that. I was offered a Lectureship at Dundee, which I turned down partly because I didn't see in terms of pharmacology that there was much future there for what I wanted to do. They didn't seem terribly keen, although they'd offered me the job. I also went to industry as well and I developed through that a very good link with what was then ICI [ICI Pharmaceuticals]. But having met them all and, particularly, Tom Blackburn, who was very junior then, we developed excellent research links that lasted many years.

**TT: Well, Tom actually came to do a PhD with you, didn't he?**

CM: Well, he did his MSc with me, while working at ICI and then he did his PhD.

**TT: Oh yes, he did his PhD with Richard Balment in Manchester.**

CM: In Manchester, yes. And then I got an interview at Nottingham where there was myself and another person from Gerald Curzon's lab, Peter Knott, so we were up against each other, and two other people. Anyway I

was offered the job and Lucilla and I decided, 'Let's go there.' There was also the possibility of going to St George's, which was where Humphrey Rang was during his short spell there.

**TT:** Oh yes, I'd forgotten that.

CM: The Nottingham move turned out to be very successful, because I went there with the strong support from the Department to set up a neuropharmacology lab. They were very supportive.

**TT:** This was a straight Pharmacology Department?

CM: No, it was Physiology and Pharmacology at that time, and it's gone through many mutations since then.

**TT:** Everywhere has.

CM: Yes. The Head of Physiology was Peter Fentem and the pharmacologist was Tony Birmingham. They were both very supportive.

**TT:** Before we talk more about Nottingham...

CM: There is a very important spell in between, because we went to America. It began when Michael Joseph and I were talking about how we might measure transmitter release and around that time, in 1977, an electrochemist called Ralph Adams in the States, published a fairly short letter in *Nature* about the possibility of using electrochemistry to measure amines. And in his lab in Kansas, he had been developing the HPLC technique, to measure dopamine, noradrenaline, 5-HT *etc.*, which of course totally revolutionised the ability to measure very small levels of the amines relatively simply. And I was fascinated by this idea that he was suggesting, that one might be able to put a very small probe into the brain and measure amine release electrochemically. So I contacted him and told Gerald that I was going to contact him; Ralph was actually in Europe at the time and on his way back to the States he came and we met in a wine bar around by Queen Square, he and myself, discussed the possibilities what one might be able to do. He was very keen, he was delighted that a pharmacologist would be interested in something that was so chemical, because he was an electrochemist of very great repute, but he had in his later years, he'd gone off to, I think, San Diego and had done a neurochemistry course at the age of 60ish, 55/60, because he felt that that was going to be the area that his approach could be applied to.

Ralph had already done a lot of work with the new HPLC technique doing microdissections of the human brain and being able to measure 5-HT and dopamine in very small regions of the brain.

**TT:** Post mortem?

CM: Yes. But he was interested, as I was, in being able to try and measure the transmitters *in situ* and, of course, I had access to the drugs that could alter release, and knew which drugs to use to try and see if we could measure changes in release. So I was going to go with Gerald and Peter Knott and Mike to a meeting in Wisconsin, it was called the 'Tryptophan Club' and the meeting was in Madison, Wisconsin. After that meeting I went to Chicago to give a talk at Loyola University, and there I met Stan Lorenz.

**TT:** This is somebody from Chicago?

CM: Yes, he was from Chicago. I had met him in Bergen, because he had been in Bergen in the Physiology Department, I think. And he said he'd drive me down because he had heard about Ralph Adams and the wonderful things that were happening in his lab, so he said could he come down to Kansas. And it's the only time I've been stopped on the road and made to get out of the car and put my hands on the top because we were speeding, going 58 miles an hour or something. But anyway, we got to Kansas in one piece, and while I was there we did an experiment with chloramphetamine, a drug that releases 5-HT, to see if we

could get an increase in the signal from what we thought might be 5-HT with this carbon based electrode in an anaesthetized rat. And the signal went up.

**TT: How exciting.**

CM: It was exciting. I've still got the original trace, you know. And the signal went up, so we were absolutely thrilled, and Ralph was thrilled and Jim Conti and Elaine Strobe, who were the two PhD-students who were doing it, were thrilled too. And so, then, I had to go home, and I went back with this trace and was able to persuade the MRC to fund the remainder of my time before I began in Nottingham on January 1<sup>st</sup>, 1978. So what Lucilla and I did - we had two children by then - we spent 8 weeks in Lawrence, Kansas doing experiments, or I was doing the experiments and they weren't having a wonderful time, because Kansas is not a wonderful place [laughs], but the experiments worked and we got a lot of data out on both, what we thought was the dopamine signal and what we thought was the 5-HT signal, using drugs that increased release, like amphetamine and fenfluramine.

And so that was very exciting and everybody from Ralph Adams' lab was excited and people who had been in his lab, like Mark Wightman, they came to see it all happening. Then I began my new job, but I came back from that 8 weeks with two things: the knowledge and skills to do the HPLC; I think probably the first in the UK to have this new electrochemical detector, and in conjunction with both a company in America and a company in the UK, the detector very, very quickly was on the market. Not with any financial gain for me of course, but they were very pleased to have an expert in the UK who knew how to use it.

**TT: So were you able to set that up in Nottingham?**

CM: Yes, immediately.

**TT: How were you funded? There was this expectation for you to set up a neuropharmacology lab.**

CM: By the end of the first year we got all the HPLC going. The funding, some initial funding came from the Department. Most of the equipment was actually loaned to me, or given to me, because we were the people who could do it, and people used to come from far and wide to see how to do amine HPLC in particular.

**TT: Who loaned you the equipment?**

CM: There was a company in Britain, they've changed names so many times, I can't remember what the original name was now. And then there was a guy who had been with Ralph Adams, and built the original box and had then set up his own company. And so they provided me with a set of equipment. We got it going and there were people in the Department at that time who were also interested, both the toxicologists and there was also Ian Macdonald who works on metabolism and diet, and he wanted to measure plasma noradrenaline, so he got involved. So there was quite a lot of interest. So that was the HPLC side, which at that time we simply used to measure amine brain tissue levels, and then there was voltammetry. Ralph Adams had given me a 'black box' with which to do 'chronoamperometry' as the technique is called, and we were able to get that going. What I did do very quickly was to get two BBSRC [Biotechnology and Biological Sciences Research Council] CASE [Collaborative Awards in Science and Engineering] awards, one with Reckitt & Colman and the other one was with ICI. That brought in two PhD-students right from the beginning, one was Trevor Sharp who is now a Professor of Pharmacology at Oxford, and of course has been an international leading light in the 5-HT research field.

And the other one was John Stolz, who did some very good work on anti-depressant drugs. I was very interested in depression at that time, though later moving more into schizophrenia; but depression was my interest at that time. So with the PhD-students came a bit of money and also some from the Department. But it was fairly shortly after I was appointed, I think 1981 that I got a Wellcome Trust Senior Lectureship, so I gave up the security I'd fought to get [laughter], which again I think in the long-term was the right move to make.

**TT:** One of the things that is fascinating about your career is the importance of techniques and development of techniques, and how you have adopted techniques or developed them. And it's always an interesting question, isn't it, whether you're technique led or ideas led?

CM: Yes, I think I was ideas-led, because I knew what I wanted to use the techniques for. We put a lot of effort into the voltammetry and on discovering that we weren't just measuring dopamine, we were measuring DOPAC [3,4-dihydroxyphenylacetic acid], and then that we were measuring also ascorbic acid and uric acid; this complicated everything. It was also very difficult to adapt the voltammetry method to the free-moving animal. That's been achieved since in the States and they've developed it and it's going well, but within a rather small group of people. And I didn't really want that. What I wanted was the ability to measure release during behaviour and that was still the driving influence. So the voltammetry went alongside the co-development of the microdialysis technique. And that all came about because I sent Trevor Sharp off to a workshop in Amsterdam on various techniques for postdocs and postgraduates, and there he met Tyra Zetterström who worked with Urban Ungerstedt at the Karolinska Institutet, Tyra was his PhD-student. Trevor and Tyra got on very well, ultimately married and had four children, but they, right from the start, saw that there was a link between the two labs, because we had the HPLC and they had the microdialysis probe, and they were still having terrible problems doing the HPLC. And so the obvious thing was for Tyra to come to Nottingham and use our HPLC, get the microdialysis going and show that it worked. With our HPLC system, it was sure to be very good! Urban Ungerstedt being a great guy was more than keen to do this.

**TT:** You had already met him?

CM: Yes, I had met him at meetings. Yes, he sat behind me when we gave our first presentation on voltammetry and he tapped me on the shoulder and he said, 'You just ruined my life, you know because you got there first' [laughter], because we had the voltammetry method. Urban was very, very helpful and Tyra came, it all worked, and that resulted in an enormously referenced publication. That's the one in *Journal of Neurochemistry*, measuring dopamine release *in vivo*, in response to *d*-amphetamine.

**TT:** And during this time, where are your concerns with mental health?

CM: Well, at that stage it was very much concerned with depression, we weren't trying to model the disorder at all at that stage, that came later with the isolation-reared rats and the link up with Trevor Robbins. But at that stage we were interested in trying to get better anti-depressant drugs, because the biggest issue was of course the slow onset of action, and so you had to wait two to three weeks. So, one was beginning to think about how one might find a faster-working anti-depressant. We were using very simple behavioural testing to test anti-depressant drugs, to see if one could identify partly the receptors involved in their action, and we were particularly interested in 5-HT receptors. At that time, throughout the 1970s and even into the early 1980s, the Americans were noradrenaline-led or norepinephrine-led to use their term and we were 5-HT-led. Our interest was the 5-HT field, and I remember talking to Ray Fuller about this, because he was always frustrated because he couldn't get his compound fluoxetine off the shelf and into the patient in those days, but then of course, later, it was an enormous blockbuster.

**TT:** You say you weren't particularly interested in modelling at that point? But you must have been using some models?

CM: Yes, I was beginning to think about it I suppose, but we hadn't really, I wasn't vain enough to think I could model depression, and still don't think I can. But I was moving towards certain ideas, such as what are the key features in the brain that are important for depression, schizophrenia and so on. What is it that goes wrong with the brain? But it took us from, when published the paper on microdialysis with dopamine in the anaesthetized rat in 1983, until I think 1991 that we published the first paper that used microdialysis in a freely-moving animal during behaviour, and that was the work with Ian Wright on the elevated X-maze.

**TT: And the freely-moving animal was another rat?**

CM: Rat, yes. And that was I think that was the first paper to show you could use the microdialysis technique in the freely-moving rat while it was doing behaviour, and we used the elevated X-maze. I don't know if you know the elevated X-maze? The elevated X-maze is a very simply model of anxiety. It is raised off the ground, elevated, and it's a cross maze. One length of the arm are open, complete no sides, and the other has a closed arm, and an anxious rat, well the normal rat will spend majority of time in the closed arms because that's where it feels safe, and it looks out of the closed arm and decides it doesn't want to go into the open arm, but it might skittle across the middle bit to get into the other closed arm, the side of the closed arm. We and Sandra File in London, she was the one who really developed the elevated plus maze as a test of anxiety, we just used it, had shown that if you give a benzodiazepine for example, an anxiolytic drug, the rat will spend more time in the open arms. And so we thought this would be a good simple model to test our microdialysis system, because the rat could run on its lead wherever it wanted to. We very quickly showed that when they went into the open arms, 5-HT was released. So exposure to an aversive situation, it's not real anxiety, but an aversive situation, produced an increase in 5-HT release.

**TT: When you say 5-HT release, where from?**

CM: Well, we looked, we had our probes, our microdialysis probes at that time in the hippocampus, they were in the ventral hippocampus. We did it in the ventral and the dorsal, and they both worked. And so we were able to show that there was a link between the 5-HT release and the behavioural situation. It's been done for lots of other behavioural situations since then, looking at 5-HT, dopamine, noradrenaline *etc.*, and a lot of people have worked on aversive situations, because several transmitters are released during aversion in various brain regions. So we jumped into the 1990s. At that stage we would link up with Trevor Robbins in Cambridge with the isolation-reared rat, which we found, very interesting. I'd become interested in early brain development because that might be the time of key changes resulting in altered mental state and mental health, and you could model some of the environmental influences that might alter brain development. And the isolation-reared rat was just an extraordinarily simple way of doing it. It's not terribly sophisticated, but very enlightening.

**TT: Would you like to explain what that is?**

CM: Yes, the isolation-reared rat is a rat that has been housed in social isolation from the time it is weaned. Rats are either kept in groups of five, socially-housed, or live on their own in a cage. Rats are social animals and interact together - particularly young rats - they play together and touch each other. What we found was a very marked difference between the rats that had been reared from when they were weaned for four weeks, or eight weeks, on their own, compared to the group-reared ones in terms of all sorts of measures. We began with behaviour. They were more rigid in their learning, they found it more difficult to adapt, they had a greater response - well they more actively sought drugs of dependence, they were more anxious, they responded more to an aversive situation than a normal rat. So, cognitively and behaviourally, they were altered. And then we began to look at the link between the behavioural changes and the neurochemistry, and the most interesting were the changes in transmitter release measured with microdialysis. For example, the rats that were reared in isolation their 5-HT did not respond to aversion, it didn't go up as in group-reared rats. The increase in 5-HT release is to alert them to the danger they're in, and that just didn't happen. And there were similar sorts of changes in other behavioural and neurochemical fields, but we very much concentrated on the 5-HT side. There were changes in the sensitivity of the 5-HT receptors. And then we've gone on to show that the factors that are important in determining plasticity, neuronal plasticity and so on, are also defective in the isolation-reared rat. They have fewer synaptic contacts, less branching of the neurons, and so forth. So they're, developmentally, a different kettle of fish. And drug companies jumped on this and have - when they were working on drugs for schizophrenia, which they've given up on at present - very much used it as a model of schizophrenia. It's much more than that, it's a model of what can happen if you're subjected to isolation during development, rather than being a specific model of a disease, I think. But it does show that a fairly small environmental change like being reared in social isolation for a period of time when you're young, if you're a rat can have a very marked effect on the development of your brain.

**TT: What was the impact of your work in this area? First of all, to other scientists.**

CM: Well, for other scientists, clearly the microdialysis work had a very large impact not just within the academic scientific community but within drug companies. Every drug company by 1990-odd had set up microdialysis often with our help and collaboration. That was very nice for us, because it kept research money flowing in. And in terms of the isolation rearing and trying to improve the level of behavioural testing that people could do relatively simply and which had translational value. It also had a big impact on the drug industry at that time as they were very much into neuroscience; sadly, they have dropped out now, but it had a big impact in industry.

**TT: Did it have an impact at the time in actually developing a good drug for anything, for clinical treatments or effect?**

CM: Well, that's an interesting thing because at the moment we are still working on 5-HT<sub>6</sub> receptors, though not me now as I've retired, but Kevin Fone and other colleagues. The 5-HT<sub>6</sub> receptor is still very much a receptor that people are very interested in as these compounds may have clinical use in terms of possible improvements in cognitive functioning, so possibly useful in ADHD [attention deficit hyperactivity disorder] /Alzheimer's and some are now in stage 3 clinical trials. Some of our work is significant in that it is the basis for the current interest in 5-HT<sub>6</sub>. So I can't say that our work has led directly, at the present time, to a drug that's become a blockbuster, but I think it has certainly improved the understanding of the mechanisms and the way some drugs work, and by doing that, this has improved understanding of their possible clinical value as well of side-effects and potential side effects.

**TT: And during this time, have you always worked principally on rats or did you move into other animals or even into clinical work?**

CM: Principally on rats and mice in recent years, because of the use of transgenic animals, which we have used a lot recently. Our most recent work, since 2008, on glutamate transporters was using mice, which we've genetically-engineered. I have done quite a lot on IBS [irritable bowel syndrome] and the role of serotonergic mechanisms in IBS in patients with Robin Spiller at Nottingham, which has, to use that awful impact factor, resulted in some highly-cited papers. And that's human studies, of course, though we have also done some mouse-based IBS work with a grant from the BBSRC, but the vast majority has been in humans. Also with Peter Tyrer, I was involved in the early clinical trials with the SSRIs [selective serotonin reuptake inhibitors] in the UK with paroxetine, and that, of course, was human studies; there we measured the changes in serotonergic platelet function. But in terms of the neuroscience experimental work, it's been animal-based.

**TT: You just mentioned then, Charles, 5-HT<sub>6</sub> and I'd just like to talk a little bit about receptors. 5-HT receptors to start. Were you at the famous Heron Island meeting?**

CM: No, I couldn't go there. One of my PhD-students went, but I didn't go.

**TT: How involved have you been with that whole receptor story?**

CM: I suppose for quite a long time my interest has been in the function of the different receptors, but not with their classification so much. People have come from drug companies and said, 'We've got this new 5-HT<sub>1A</sub> or <sub>2B</sub> receptor, what do you think its function is? You're the person who might be able to help answer that.' So I haven't been involved in the classification, and because I'm not a molecular biologist, one of the difficulties during the 1980s for somebody like myself - who is very much interested in function and whole animal work and trying to model behaviour - was that this approach was not seen as very sexy at that time. You had to be a molecular biologist and be doing things very, very quickly and also the Government at that time liked a quick turnaround. But I was lucky and very much protected, because I was funded by the Wellcome Trust throughout that time, and my funding was continued throughout, so I was able to maintain a behavioural whole animal approach, which became very run down in the UK at that time. But then, in the

1990s, when the transgenic animals came, everybody wanted functional work. They wanted to be able to do decent behaviour, and so there was Trevor Robbins in Cambridge and ourselves and so on, who still had that ability. The group in Bradford also. There weren't a lot of us around at that time.

And so I was very lucky, I was very grateful that the Wellcome Trust have actually allowed us to keep going or else we would have had to change direction and drop our approach. I think I was funded directly by them for 11 years, certainly my salary was until basically the Wellcome scheme came to an end.

**TT: And you've talked about the money coming in from drug companies. This was mainly for students, was it?**

CM: Well, not just students, but also for projects and postdocs. I had a lot of BBSRC studentships and PhD-students over the years, I think 70+. A lot of those were BBSRC studentships. I always collaborated with other people, and if they were with industry, of course, they would have had an industrial supervisor as well.

**TT: It's an astonishing list. I want to come back to it at a later stage to how you divided your time between all your activities. Can we just go back to the collaborations you had with drug companies because you're quite unusual in having had a completely academic career. An awful lot of people dip in and out of academia and industry. First of all, were there never any approaches from people saying, 'Come on, Charles, come over'?**

CM: Yes, there were. But I was very lucky as Nottingham had excellent facilities for what I wanted to do. I had a superb animal facility, and over the years we had been able to build up specific behavioural labs for rats and mice, all separate, all computer-controlled and monitored, you know, for behaviour and so on. It all became quite sophisticated really and that became something very hard to give up, because it was going so well, it was an interesting place to be. I loved the research, I liked the people I worked with, and I had great colleagues. We got on really well and the money continued to come in. I did a lot of collaborative grant applications so we had money from the Wellcome Trust, the MRC, the BBSRC. And also some postdoctoral fellowships from industry as well which were not related compounds at all, they were just pure research, particularly with GSK [GlaxoSmithKline].

**TT: You seem to have had a lot of collaborations with GSK. Quite a few of your students...**

CM: Went to GSK, yes. I had one extraordinary time when we were having a meeting with GSK at Harlow about a schizophrenia project, and how we might develop a better drug that could treat the cognitive symptoms. And there were 10 people in the room and I think 8 or 9 of them had been through my lab [laughter].

**TT: Were you the 10<sup>th</sup>?**

CM: I was the 10<sup>th</sup>. It was a bit incestuous really.

**TT: That's an astonishing achievement. You must have a quite specific desire to supervise PhDs or to have PhD-students in your lab.**

CM: Yes, I liked to have three on the go a year and so I would take up to three a year. Also I do think it's a very important part of an academic's life training the next generation. I had battles with a guy in the Department about this, because he said 'PhD-students are a total waste of time. You've got to train them, you've got to teach them, you've got to educate them. There's no point, you may as well just have a postdoc.' And I always argued, 'Well then if you only are yourself and the odd postdoc then what have you left behind when you leave? With PhD-students you can look around and say 'I have achieved something by training some good people who have good jobs.'" And he then became the Head of the Department and his attitude completely changed and said, 'We've got to have PhD-students,' because it meant money, money, money. I think I was very lucky as we got good PhD-students both from the UK and abroad. We developed a good

reputation and, also, we had at various stages, different places where they came from. We had a lot from Bath at one time who were very, very good.

**TT: Was that when Rod (Flower) was there?**

CM: Yes, around that time, and also just after that as well. There were some very good people at Bath, and they came, and they knew what research was about. I also think the BBSRC scheme, as it was then, the CASE award scheme was very good because it did give them experience of both sides. It gave them the chance to have a project that they could use both an academic approach, combined with the ability of industry to provide aspects that we couldn't provide, because they were just too expensive. I also had quite a big international link as I represented the University in South East Asia, particularly Thailand from where we had some excellent PhD-students. In the end, from about 2000, we've had a joint medical degree with one of the universities in Bangkok that I developed with a very cheerful and positive Thai colleague. The students do their preclinical years in Nottingham and the clinical years in Thailand and that's gone from strength to strength; now one of my closest colleagues at Nottingham, Vince Wilson, runs it brilliantly. The Faculty was keen, but they were a bit wary of it to begin with. Nottingham traditionally had a big intake of international medical students, one of the biggest in the country. I think we had 24 a year, and the Thai students were not part of that quota, as they did not do the clinical course in Nottingham.

**TT: Why was that?**

CM: I don't know. It was a historical thing and I was involved as myself and another colleague, a clinician, we were responsible for the selection of the international medical students, and we used to go out to Malaysia and Singapore to interview.

**TT: Because Nottingham is a comparatively young Medical School?**

CM: Yes, it had this big intake, it was 24 a year, of course in the recent years this has been cut by the Government. But Nottingham still has a generous number of international students in the Medical School, because of our joint medical degree, and they are not treated as clinical students. They're treated as non-clinical undergraduates, because they do our BMedSci degree as do all medical students at Nottingham, so the Faculty is more than grateful now and they want more and more of them.

**TT: Can I just go back to your amazing list of PhD-students? I think you've got somebody in practically every drug company.**

CM: Yes, well but the jobs listed are mainly their first jobs. I haven't kept them all up-to-date.

**TT: What do you think about this legacy you've left? There's quite a few who have gone into medical journalism?**

CM: Yes, that's interesting. Most of those who did that had specific reasons. John Stolz was one of the very first PhD-students, and he now has his own company, but he went in because his wife became very ill and he found that he could do it from home; also he was very good at writing. Another reason for example is Ian Wright, he was a very able student, but became terribly allergic to animals of any form in labs. A surprisingly large number do become allergic. So Ian decided it was the best thing he could do. There were others who just wanted to do it. Savvas Neophytou who is down in the list as Finance ended up in the City here. He is a Greek Cypriot, and he was again very good and produced some very good research, but I think he was always interested in finance as well and doing a postdoc, and then he became a finance guy who knows all about drug companies and drugs.

**TT: Do you feel disappointed if your students leave the lab, if they go into alternative careers?**

CM: Not really. Some you feel it's the best route [laughs]. You probably know the feeling. But some you think it is the best thing for them. The international students, the ones from abroad, are all in academia and many have done extremely well. There are you know some who have done very well now. Trevor [Sharp] of course, is Professor of Pharmacology in Oxford, and then there's Emma Kidd, she has a senior position at Cardiff and Nigel Maidment, Joe Cheer and Danet Lapiz have excellent academic positions in the USA.

**TT: Some people think they've failed if their students leave the lab, whereas I think you are surely raising scientific literacy in the community...**

CM: They know about science and they are usually in areas related to science. I think to have a PhD and know how difficult it is to get reliable research information makes them useful in a lot of related jobs. You hope as a supervisor that they have all developed their critical abilities and in particular their abilities to assess information, which I think with the internet these days, has become more and more important.

**TT: Absolutely, yes. As well as this impressive list of PhD-students, a quite astonishing item in your CV is what you might call 'service'. The Faculty and University Committees, the Societies, and the Editorial Boards, some of them of very long-standing. You joined *Neuropharmacology* in 1982?**

CM: Yes, it's been a long time.

**TT: How do you manage to fit all of these things in?**

CM: Well, University Committees are not terribly taxing. The advantage of being on those University things is that you do get to know what's going on in the University and who is who, and that I found very useful, to actually be on fairly easy speaking terms with the Vice-Chancellor is not something that is un-useful and the same with the Pro-Vice-Chancellors and others. The fact that they know who you are, I think, is quite helpful. Plus, I find people very interesting. I find students very interesting, whether they're postgrads or undergrads. I really did enjoy the teaching side of my job and I never gave that up. Some people suggested I could have dropped all my teaching when I had my Wellcome Trust Senior Lectureship, but I said 'No, I wanted to develop a neuroscience teaching' both to the medical students and then, ultimately, we developed the first full neuroscience degree in the UK. I was always very pleased that we did that and it's worked very, very well. Now it's extraordinary as the drug companies have given up neuroscience, but young people haven't given up neuroscience. We began with an intake of 12 and they all went on a placement. Some science subjects have lost impact, genetics has crashed. I don't really know why it's gone down, apparently it's gone down a lot - there's less interest in genetics. In neuroscience, we are now seeing more and more good students and those concerned with 'student numbers' say 'Oh, we don't have to worry about this because neuroscience can just take more, they've always got good students,' and the people who run the course now are really getting worried, because there are now up to 70 students a year taking neuroscience, so this will put a real strain on the quality of the course.

**TT: And what about the editorial duties?**

CM: Yes, I was involved with *Neuropharmacology* for a long time and edited special editions on ADHD and 5-HT. I found reviewing articles quite interesting; it was very much a learning process as people would write things in different ways and, I think, also the fact that I don't think I am a person who particularly bears grudges or is antipathetic towards certain aspects of things. I think I was fairly even minded in the way I dealt with the reviewing process. I've obviously been at the other end where you've had people who have really gone for you and quite unnecessarily I often thought; I felt it was job that I should do. I now, together with Mark Geyer, Bart Ellenbroek and Thomas Barnes are editing a series of books called '*Current Topics in Behavioural Neuroscience*', which we've got up to volume 33, and we just had a meeting in Florence the week before last, and there is a really interesting issue about such publications. They have been enormously successful in terms, not in terms of sales of the whole hard copy books, but the individual chapter and whole book downloads are incredible. Combined, they run on average to 35,000 per volume and the one on addiction

went up to 50,000 or something. And, yet, that exposure, in terms of the research assessment exercise is considered to be meaningless.

**TT: Yes, we have a similar problem with our Witness Seminars.**

CM: Yes, I'm sure.

**TT: We can have 100,000 downloads but that's ignored, because we haven't sold 200 copies of a conventional book.**

CM: We're trying to get Springer now to break it down too, because you can download the whole book or download a chapter, and then if we could break it down, then we could make a stronger case to argue.

**TT: I think people are increasingly having this problem. People are moving into electronic publishing. The other thing in terms of academic service is learned societies. So I want to ask you about two organisations in particular. The first is the BPS. When did you join the BPS?**

CM: Now, when did I join? I think I gave my first communication in 1969 so around then.

**TT: What was your first communication on?**

CM: It was on COMT, it was when I was in Norway, and because Hans Cato Guldberg had been in the MRC in Edinburgh and was a Member, he came to maintain the contact. I had a very nice Chairman, and there was a person that I really admired in the front row, Hermann Blaschko who was a lovely, lovely man, and he asked very nice questions. He was very incisive but asked good, fair questions. And I had been viva'd by him for my MSc degree at Southampton. And like everybody says in those days, there was a whole front row of very famous people. I never had a bad experience with the BPS. I haven't given a communication there for years, but the same applies for my students. We always used to encourage them to present at the BPS. We would rehearse them through an n<sup>th</sup> degree, but they all found it a positive experience. I never had a student savaged, like one witnessed in the past at the Phys Soc [The Physiological Society].

**TT: Oh, blood was drawn there, yes. I remember my own first communication to Phys Soc and yes, you look at the front row and they're all Nobel Laureates. Terrifying.**

CM: Yes.

**TT: But you seem to have much more of a involvement with the BAP?**

CM: Yes.

**TT: When did that come about? Was that at the same time or was that earlier?**

CM: The BAP began later and the BAP didn't exist when I joined the BPS. Richard Green's just writing, or has just completed a history of the BAP. I was certainly loosely involved in the BAP in its early days. I then lost a certain amount of interest, but it went through a difficult phase. It was very much taken over by clinicians from its early days. It wasn't initially, but then the clinicians stepped in rather heavily and they had meetings in the Channel Islands and things like that, which I didn't approve of. Anyway, I then got involved, it was David Nutt who said that 'You know, it's time you came into the fold, it really has improved,' which it had by then. I joined the year I got elected onto Council. I think that I joined in 1990, and was elected that year onto the Council.

**TT: What is it that appeals about the BAP?**

CM: I think it was the mixture, partly it was the mixture of clinicians and basic scientists, and the aim was strongly that there had to be communication between those groups. And so all the meetings were organised with that flavour in mind, but we, as scientists, needed to talk to clinicians. I've always supported that view and, of course, the clinicians who were involved in the BAP are very much academic clinicians, so they are more like a basic scientist; it's an easy communication to have. But, I think that was the main aspect that appealed to me, together with the excellent atmosphere of the Association. They have a very good meeting once a year and I felt that there was increasingly a need to put across the importance of psychopharmacology and the use of drugs in psychiatry. There is a school of thought, I'm sure you know, that all drugs are bad. But I don't hold to that view at all. Not just because I'm involved in drugs, but because I have seen throughout my life the benefit of good treatment by good psychiatrists.

**TT: I don't know much about BAP, I've never been to a meeting, so could you describe, is it a similar meeting to say the Phys Soc or the Pharm Soc [BPS] where people submit papers?**

CM: Well, yes. What they tend to have is organised symposia in the morning followed by plenary sessions, themed poster sessions and themed oral sessions and on one day there is a symposium organised by postdocs and also a session when the BAP prize winners present their research. They have one big meeting a year, and that lasts three days.

**TT: And as Meetings Secretary and Programme Secretary, Membership Secretary, President, what was your role in developing the themes?**

CM: Oh, very much in terms of what themes, we don't have a fixed list of themes, the themes each year are those themes created each year depending on what proposals come in from the membership. Actually, to put the programme together was one role, and particularly reviewing all the abstracts for the poster and oral sessions. We make sure that none of the posters are just drug company propaganda sheets; there's always quite a big blitz to avoid that, because that has been a problem in the past. The abstracts must contain real research.

**TT: And so, particularly, when you were hands-on doing this, were there any particular themes you really pushed yourself? What I'm really trying to get at is, has your involvement with the BAP, has there been synergy between that and your own research career, and the ideas and the things that you have thought are important?**

CM: Yes, I suppose some of the time. I've been very keen to bring in things like brain development and environmental factors. It's a difficult process, because there is a move now away from just talking about schizophrenia, and rather than talking about schizophrenia discussion is about the cognitive aspects of schizophrenia, the social aspects, and you actually do completely move away from talking about depression, anxiety or schizophrenia and break those up into the behavioural characteristics with which they are associated, and you find a lot of cross talk between the specific disorders. And I think the BAP has gone some way along that line. There are certainly some clinicians, particularly, who feel happier to stick with depression, but depression is a cognitive disorder as much as schizophrenia is, and there may be a lot of cross talk there. So how you break it up, I think, is an important question, and certainly we have begun to do that.

**TT: Are there any that you are particularly proud of organising or you think, 'That was really innovative or really worked,' or you're surprised that something really interesting came out of a meeting?**

CM: With the BAP they tend to be very successful, informative meetings. There is now an increasing feeling that we need to put across the problems that psychopharmacology, and pharmacology in general, though psychopharmacology in particular, are facing in terms of the lack of interest by drug companies and relevant psychopharmacology research. And so, I think, in the last few years there has been a much greater effort to try and not just have the drug companies there because they want to sell their drugs, but to bring them into

the core in terms of having open plenary sessions that deal with these issues, and to get them to say why they're not involved in such research. I think that that's been successful.

**TT: Was that a quite deliberate, conscious move to do that?**

CM: Well, that was really in the last few years and there has been a conscious move to do that. I think one of the great strengths of BAP has been their guidelines, and their guidelines are very widely used.

**TT: Ethical guidelines?**

CM: No, treatment guidelines. Ethical guidelines is an interesting one and we have discussed that and actually in our book series [*Current Topics in Behavioural Neuroscience*] we have produced a volume on the ethics of behavioural testing in humans and animals.

**TT: Well, that brings me onto the next question, one of the things that you've mentioned in your CV is the Research Defence Society.**

CM: Yes, which now is essentially changed.

**TT: Yes, it's now Understanding Animal Research. I was there last week in fact. You've worked on rats all your career, so I want to ask you about animal rights. Have you ever had any problems from your work?**

CM: Not violence in any way, we had protests and so on. I was, together with Trevor Robbins and one of my collaborators, we were named by the, was it the *Daily Mail* or was it *The Mirror*, as the most useless people in the world for our research on the isolation-reared rat.

**TT: Useless?**

CM: Useless people in the world or something, yes. One of those awards made by the media and given for our work on the isolation-reared rat model. And interestingly, I asked the University, because I didn't respond and took it at face value so to speak, whether there should be some response from the University and they were very, very reluctant to do anything. I mean they'd been very supportive of animal work, but not in terms of responding. I understand people's views, my eldest brother was extremely opposed to what my research was, but it hasn't affected our relationship. I know he doesn't like animal work. I'm not quite sure why, and I have tried to argue with him why. I think there is an issue, and it has become more apparent, but we have tried to address it. I wrote a paper with one of my postgrads, it was a review for a special issue on MDMA [3,4-methylenedioxymethamphetamine; ecstasy], and it was about the translational value of animal *versus* human work. I'm sure you've spoken to Richard [Green] about this, there is an issue about the translational importance with some of the animal work to human work, and that's why I'm very conscious of saying with the isolation-reared rat, much as the drug companies like to call it a 'model of schizophrenia', it is not a model of schizophrenia, as we are looking at the development of the brain and how it is influenced by environmental factors. And that may be of real importance in terms of our understanding what might happen in the human brain. And there are parallels there. We know that maternal deprivation is very harmful. You only have to look at the Romanian orphans' study from the Institute of Psychiatry to see that.

**TT: Sir Michael Rutter's work.**

CM: Rutter, yes. Yes there are lots of parallels with our isolation-reared rat. The same bits of brain are affected and so on. And so what we're trying to do, is to get understanding of what might happen. And it's interesting with the isolation-reared rat if you touch them, you handle them every day, you don't get the effects. It's all to do with contact.

**TT: One final question: could you say something about the ‘Monitoring Molecules in Neuroscience’ group?**

CM: One of the key things when you have a new technique, I think, or a new approach, you can either keep it to yourself, or you can expand it and let everybody get hold of it. With the development of the electrochemical HPLC technique for measuring the amines, we were very keen to make sure that it was widely available. And, so, we began a meeting in Nottingham, I think the first year was 1982. That was only within a year or so of us getting it going. And then we held other meetings after that, but after, I think, the third or the fourth one, we decided to expand the scope and we came up with the idea of ‘Monitoring Molecules in Neuroscience’, which would be all-embracing for everything - not just HPLC - but all the emerging techniques. And that attracted a lot of attention and a lot of people came, and we had a very successful event in which one of the people who came was Urban Ungerstedt and his plane was late, so in order to get to Nottingham in time to give his talk he hired a Porsche at the airport, which was quite amusing way to get there. That’s his character. Anyway, since then those meetings have been held every two years and they still continue to this day, and the next one is actually this year in May 2016 in Gothenburg, Sweden. And they tend to alternate between Europe and America. The last one in London was in 2010, I think, which was held at the Royal Geographical Society building. So it’s been an excellent way of bringing people together.

**TT: Which people?**

CM: Well, both the experts in the techniques, but also the way in which they’re being applied, both in basic science and in clinical science. So both in animal and in human research. One of the things that I got involved in in the latter years at Nottingham, about 2000/1998 I think, we, together with Peter Morris, who is the Head of the Sir Peter Mansfield [Imaging] Centre at Nottingham, obtained a large grant to set up a small animal fMRI [functional magnetic resonance imaging] and MRI [magnetic resonance imaging] Unit from the MRC. We were able to do that because Zeneca, who were based in Knutsford in Cheshire, were going to get rid of their magnet of a suitable size, so we got the magnet from them and all the rest of the money from the MRC and that is, again, I think, one of the first applications of fMRI to look at the effect of drugs in different brain regions to try and identify where the drugs might specifically be acting and whether procedures such as the isolation-reared rat only produced morphological changes in the brain, which we were able to measure with the MRI, but also produced functional changes in response to various drugs in the brain. This is an approach that has really all come out from Monitoring Molecules and is of one of the things that is still covered by our Monitoring Molecules in Neuroscience approach.

**TT: And of that membership or of that group, have there been a consistent core group of people who come to all of them?**

CM: Yes, the initial group, core group, which was very much in the UK was myself and Michael Joseph, Ian Macdonald in Nottingham, Ziggy Crook in Portsmouth, and Marianne Fillenz in Oxford, we were the main core group. They’ve all really moved on now and luckily younger people have come to take over the role and maintain the interest and enthusiasm for bringing together the people who are interested in trying to understand how function can be monitored in the brain.

**TT: Didn’t Marianne Fillenz, who died recently, work with Blaschko, or am I getting confused?**

CM: No, I think she did. She was more interested in noradrenaline and was in the Physiology Department where she did a lot of voltammetry and development of voltammetric techniques. There were people from her lab, some who then stayed in the UK, some went back to Ireland, and they have maintained their interest in this group.

**TT: Thank you for taking part in this exercise.**

[END OF TRANSCRIPT]

**Further related resources:**

1. Overy C, Tansey E M (eds) (2013) *Drugs Affecting 5-HT Systems*. Wellcome Witnesses to Contemporary Medicine, vol. 47. London: Queen Mary, University of London.
2. Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Blackburn, Tom: transcript of an audio interview (22-Feb-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016045. London: Queen Mary University of London.
3. Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Green, Richard: transcript of an audio interview (17-Dec-2015)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016034. London: Queen Mary University of London.
4. Tansey E M (intvr); Tansey E M, Zarros A (eds) (2016) *Marsden, Charles: transcript of a video interview (19-Apr-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016083. London: Queen Mary University of London.
5. Wightman R M, Strope E, Plotsky P M, Adams R N (1976) Monitoring of transmitter metabolites by voltammetry in cerebrospinal fluid following neural pathway stimulation. *Nature* **262**: 145-146.
6. Zetterström T, Sharp T, Marsden C A, Ungerstedt U (1983) *In vivo* measurement of dopamine and its metabolites by intracerebral dialysis: changes after *d*-amphetamine. *Journal of Neurochemistry* **41**: 1769-1773.