

## **ORIGINS of NEUROSCIENCE**

### **Derek Richter**

#### **Can we begin with the clash between Adrian and the electrophysiologists on one side and Feltberg and the biochemists on the other?**

Well, I went to see Adrian in Cambridge because I was interested in getting a physiologist to help me by co-operating in research on the fate of adrenaline in the body. That was a problem which Hopkins had suggested I might take up, but Adrian seemed not at all interested in a problem of that kind. He said that the physiologists didn't want biochemists working with them. That was his attitude. Working in his lab though was somebody who was from Germany, Hermann Blaschko.

Blaschko had just a little room with a large Warburg in the middle and very little room in it. Adrian said well maybe as a refugee he would be foolish enough to go into a problem of that kind. So, I went to see Blaschko and found that he was really full of interest in the problem of adrenaline. He was quite prepared to co-operate and ready for us to work together.

#### **Tell me about the work you both did. How did you stumble on monoamine oxidase?**

We agreed to see what happened to adrenaline in the body. Blaschko had already started to see if adrenaline was oxidised by any enzymes and he found that it was oxidised, but he didn't know what the enzyme was.

Since I had been working on enzymes, I was able to go into that in detail and identify the enzyme and isolate it. I was naturally interested in this and I managed to get a number of other amines and found they were all oxidised by this same enzyme which I purified. They all produced aldehydes and were oxidised in the same way. This was clearly a quite important enzyme in several different organs including the liver and the brain. It was a new enzyme which had not been identified at that time.

#### **Reading your book *Life in Research*, I noted that Judah Hirsch Quastel was also working in this area and came to see you at that time**

Yes, he came to see me because he had heard of the work I was doing on amines and he was also interested in enzymes in the brain. He told me that the enzyme that oxidised adrenaline was quite different from the enzymes that oxidise other amines. In fact, a student who had been working with him had shown him they were different, and he just wouldn't accept what I told him. So, then I fished out the competition experiments I'd been doing, showing that they were all the same enzyme, and he was forced to realise that that was true. I saw that he was working in the same field, so I immediately sent my paper for publication. Then a month or two later out came a paper from Quastel putting forward the same view that it was only one enzyme but not mentioning the contact he had had with me. I'm afraid that's the truth, but it didn't matter, since my paper had come out first. Those I knew recognised that I had been the lucky one in identifying this enzyme, the monoamine oxidase (MAO) as we called it in due course.

#### **Why were people like Adrian so antagonistic to the neurochemical view of things?**

I think that was partly Adrian's personality, because I found that he and Feltberg, who was a neurochemist, were not even on speaking terms. They were communicating only by writing. Adrian liked to feel he was running things as a physiologist, and he was not prepared to accept these biochemical mechanisms. That was the situation as I saw it.

**Reading an article by Blaschko based on a talk he gave at a meeting organised by Silvio Garattini on psychotropic drugs in Milan in 1957, that you also attended, he said that he thought what was involved was a replay of the turn of the century controversies about the role of the neuron - with one group arguing that communication between neurons was continuous and the other arguing that neurons**

**were contiguous rather than continuous and that communication must involve quanta of something in some way. Any thoughts?**

Yes, I think it was as you say.

**Feldberg isn't a name one hears of much now. Do you want to give me your view of him and his work?**

Yes, Feldberg did a fine job in collaboration with Dale and other colleagues in showing that nerve stimulation produced the release of acetylcholine at a number of mammalian peripheral synapses. He helped to establish the role of acetylcholine as a neurochemical transmitter, a view that was unacceptable at that time to many of the physiologists, who regarded neurotransmission as primarily an electrical process.

**Marthe Vogt was also in Cambridge at that time at the Animal Research Centre at Babraham and later John Gaddum. That was quite a galaxy of talent. Can you tell me more about them?**

Those of us who were working at Cambridge were certainly lucky to be able to contact such an able group of scientists who were there at that time. Marthe Vogt I got to know well, since she was studying the distribution of norepinephrine and the other amines in the mammalian central nervous system. She told Pergamon Press of the need for a neurochemical journal and gave them my name as a person who could help them to start it. That was the beginning of the Journal of Neurochemistry, which I helped to run for many years.

Gaddum was also engaged in studying the roles of amines such as tryptamine and serotonin in the central nervous system, and he was especially interested in the mechanisms involved in the processes of learning and memory. At our informal laboratory tea meetings, memory was a problem that often came up for discussion, but at that time there was no book which brought together and described, in simple terms, the work on learning mechanisms which had been carried out. I therefore invited a group of six colleagues, including Gaddum, to join me in drafting chapters for a little book Aspects of Learning and Memory, which dealt with different aspects of the problem. I was glad that the book, which was published by Heinemann's, was well received and translated into other languages, including Japanese.

**Where did Henry Dale fit into all this? He also worked in Cambridge at one point**

Henry Dale was a leading physiologist who stood out as a supporter of the neurohumoral hypothesis, that neurons are fired by the liberation of quanta of transmitter substances at pre-synaptic junctions. Dale and Feldberg and their colleagues established, in the early 1930s, that acetylcholine is liberated at a wide variety of mammalian peripheral synapses, and Dale was the one who put forward the first principle, that a cell acts by the same transmitter at all of its synapses. It was after his appointment as Director of the National Institute of Medical Research at Mill Hill that Dale wrote expressing an interest in my work on adrenaline ester and inviting me to carry out some further experiments in his laboratory with a Canadian colleague Dr Macintosh. I was pleased to accept his invitation and glad to find him a most impressive and likeable person. It interested me that, in spite of his many commitments as Director of the National Institute, he found time to join us in the laboratory and assist by giving anaesthetics to the animals on which we were working. Those experiments confirmed the inactivation of adrenaline in vivo by the formation of an adrenaline ester.

**With the work of Henry Dale and the Babraham group, I'm surprised that people like Adrian and Eccles could still discount the importance of chemical neurotransmission as comprehensively as they did. They just didn't seem to want anything to do with it**

I think the physiological approach had been going on for a very long time, whereas biochemistry was a relatively young science at that stage and I think that's really the reason. They simply hadn't let it into their field.

**Even as late, though, as 1961 in books like The Living Brain by Grey Walter, there's still a resistance to the idea. They say okay there are some neurotransmitters in the brain but they are not really important, they're just another way of mediating electrical neurotransmission. There seems to be a very deep-seated antagonism**

I think they didn't appreciate the relevance of neurochemistry in those days. All the books on the subject dealt with physiology and they regarded simple chemical factors as of no real importance. I think that was the attitude.

**There wasn't anything in it of the idea that electricity was somehow more spiritual, more ghostly than chemicals was there?**

I don't think they thought of it as being spiritual. I think they thought it was the thing that mattered. They were not interested in where electricity came from. The biochemical aspects of things seemed to them a long way out of the picture.

**When did things really begin to change, because in the meeting you organised in 1950 and in the 1953 Tanner book, where there's an interchange between yourself and Joel Elkes and a few others, and Marthe Vogt had very recently reported the discovery of noradrenaline in the brain, there was a feeling from the way you were all talking that things had changed at that point. Would you say that?**

It was changing and had changed for us already but not for those elderly physiologists who had grown up in another field.

**Can I take you back to Quastel. Tell me more about him because he was an enigmatic kind of character in a way wasn't he. Working in Cardiff, very isolated in some respects, very concerned about his reputation?**

Oh, he was doing fine work at Cardiff and he developed a group there who were working with him. I can't speak too highly of him, but of course when the War came on he was forced to move and so that was the situation.

**What led to his move?**

His laboratory was in a hospital that was being taken over for military purposes and where it would have been hard for him to continue doing research.

**Why did he leave and go to Canada, was it the lure of money and more resources?**

I don't think it was just money. No, I think he was trying definitely to be helpful by developing the neurochemical approach in particular. He accepted the invitation to go to Montreal because he was offered good research facilities there and, in due course, he was appointed University Professor of Biochemistry.

**Who were the other people who helped move things forward? In your book you mentioned Frederick Golla as being someone who was interested in how aspects of neurophysiology could be applied to mental illness, which seems to have been a different attitude to that held by Adrian and people like that who were pure physiologists and weren't so concerned with how these things might actually be applied. He seems to have been one of the people who, unlike Adrian, was interested in how emerging neuroscientific ideas might apply to mental health or mental illness**

Yes I agree there. It was Golla who first invited me to the Maudsley a long time ago and helped to develop there the biochemical work which I was doing. I think Golla was a superb person. In fact that was why I put together that little book Perspectives in Neuropsychiatry in his honour.

**What motivated him do you think? Why did he take the approaches that he took?**

After his earlier studies on the speed of conduction of a nervous impulse, Golla carried out pioneering work on electroencephalography, which he was the first person in this country to apply to the study of mental illness. As Director of the Central Pathological Laboratory at the

Maudsley Hospital, he brought together a group of scientists working in different disciplines. Together with Grey Walter, he studied the EEGs of patients suffering from epilepsy, cerebral tumours and mental disorders of different kinds. Later he moved to Bristol, where he became the Director of the Burden Neurological Institute, and he developed there a leading research Unit dealing with the problems of mental illness.

**Who joined him there? I've come across names like Hemphill and Reiss - but that was later I think**

He was joined by several of his colleagues from the Pathological Laboratory at the Maudsley. Grey Walter did outstanding work on the electrical activity of the brain, and he improved the quality of the EEG equipment commonly used at that time to study the condition of mental patients. Hemphill and Reiss studied endocrine factors such as hormone levels in patients suffering from conditions such as manic-depressive psychosis and schizophrenia.

**When you moved to The Maudsley you said that it was at the invitation of Golla, but one of the people who seems to have impressed you when you were there was Edward Mapother**

It was Mapother who brought the clinical psychiatrists at the Maudsley together with a group of able neuroscientists working in different specialties, so that The Maudsley became recognised as a leading centre, not only in this country but in the world, studying the causes and treatment of mental disorders.

**Who else was in The Maudsley when you were there?**

There were a number of active psychiatrists such as Eliot Slater, who had a special knowledge of genetics, and William Sargant, who studied the action of drugs. Others included Aubrey Lewis and Maxwell Jones. For me it was a new world, a completely new atmosphere that I enjoyed. In Golla's little lab I had the opportunity then of building things up, and that's what I was doing there. We started on the problem of young addicts. There were a lot of youthful addicts coming in and so I did work on identifying the drugs they were taking by testing their urine and things like that. Finding out whether some of these youngsters were still taking drugs or not, when they said they weren't, was an exciting problem at the time. I was also interested in more basic research into the mechanism of amine actions and other things in the brain.

**You described the formation of adrenochrome. Do you want to tell me more about how that came about?**

It was while working at Cambridge on the oxidation of adrenaline that I isolated the red oxidation product and determined its chemical constitution. I proposed that it should be called 'adrenochrome'.

**When did you move up to The Maudsley?**

In 1938, but before long the war started and I had to move out. I had got my family into a flat up by The Maudsley and I had to move them away. So I got a house in Epsom which I rented for the family because of the danger of London being bombed. While there I moved my equipment into a small lab in the West Park Hospital. It seemed that the best thing I could do there was to finish off some of the lines of research I had started on the fate of amines in the body, and in particular the fate of adrenaline. I found, in experiments on myself, that after taking a dose of 10mg adrenaline by mouth, my urine contained a compound with the properties of an adrenaline ester. At that time that was entirely new and, wanting very much to get enough of this new compound to find out its chemical constitution, I decided to take a large dose of 30 mg of adrenaline. I knew this was risky and it made me acutely ill for a week or two. However, the experiment worked in enabling me to get evidence that the compound was a sulphate ester of adrenaline. In that way a new route for the inactivation of adrenaline in the body was established.

### **You worked at Mill Hill during the War?**

Well, the thing was, the War being on, I had to consider what I was going to do and, as I mentioned in my little book, my family were against wars. My grandfather had left Germany because he was against wars, my father was anti-war, but I felt that something had to be done, and so in the end I volunteered to fight. When I came up for the normal medical investigation with a great crowd of people all of the same age, there were various tests and there was one little mental test that came out. I did it without thinking and filled it in, and it was at the end of the medical meeting that somebody came and shouted out my name. I went up and they had the little sheet I had filled in with the answers to the questions.

Apparently I had answered practically all of them correctly, which was quite unexpected and unusual, and so they wanted to know something about my background, where I came from and so on. The Ministry then sent me a letter saying that in view of my academic qualifications I would not be asked to join the fighting forces but was wanted to do things back in this country.

So, I then waited to see what I was to do. It was while waiting and living out in Epsom that I looked in at various Epsom hospitals and moved around, and then I was invited to take over the directing of a research lab at the new Mill Hill Emergency Hospital, which was at the old school that they had taken over. There at the Mill Hill Emergency Hospital I met people like Aubrey Lewis and others, and they invited me to join in the various research investigations that were going on with the military patients who had come there from the front. They were mainly effort syndrome cases who had had a terrible time out at the front and who were being investigated. That was the main job. I developed there a little research lab and brought in a few other scientists who could help.

A junior research worker Margaret Lee agreed to join me there, and then I was joined by Phillis Croft and others. And so I found myself for the first time in charge of a small Unit dedicated to clinical research.

### **You mentioned Maxwell Jones was there**

That's right. I did research with him and he interested me by starting group therapy there for some of the patients. It was not done in other places, but he brought quite large groups together and did group therapy, which he invited me to come to just to see what he was doing. My main work in collaboration with Maxwell Jones was in tests with a bicycle ergometer on changes in lactate and glucose levels in patient's blood.

### **Linford Rees was there as well?**

He looked in at times but he wasn't working there.

### **What were you doing in the research labs at that time?**

Well I was helping the clinicians in their investigation of patients, finding out about the various changes in their bodies. In looking for factors that might be related to the activity of the nervous system, I measured serum cholinesterase levels of patients, and we were interested to find it higher in effort syndrome patients than in controls. In collaboration with Russell Frazer, I studied the effects of adrenaline on the blood glucose level and other characteristics of patients. We were especially interested in the effects of anxiety and, by staying up some nights, I was able to observe the effects of anxiety induced by air-raids, which were happening almost nightly at that time.

### **Did you return to Cambridge after the War?**

During the War, while I was working at Mill Hill, I managed to get my family moved to Cambridge. I didn't want them to live at Mill Hill, where there was bombing danger, so I took a house in Cambridge for my wife and family. I went back there most weekends, not every

weekend but a good many weekends. A German invasion was threatened and since I thought of the young children in our house and the necessity for food for them, I bought an allotment in Cambridge to produce food for the family. So, I discovered my first gardening interests.

**At the end of World War II, what state was research in in the country? There had been quite a bit of fairly important work done before the War - the adrenochrome and amine oxidase work - did the War put an end to all that?**

During the War many of the research laboratories closed down. There was a little research on war-time problems, but basic research had practically come to an end. Since my work at Mill Hill involved largely dealing with patients, I felt it was necessary to get medically qualified. The authorities generously allowed me to spend part time studying anatomy at Cambridge and then taking the medical course at Barts. At last in 1945 I got through my final medical exams and became medically qualified. That was the end of the War and so, to get more medical experience, I took a post as House Physician at Addenbrookes Hospital.

After that, I felt that I must be getting back into research. I looked for jobs and I decided to take one which had been Quastel's job at Cardiff. So, I went to see Hennelly, the Physician Superintendent, who was in charge of the Whitchurch Hospital, including the research laboratory there. The lab I was given was clearly run down, since it had not been used for several years, and my first task was therefore to get it set up with modern equipment.

I was surprised to find that Hennelly also put me in charge of two admission wards, where new patients were coming in from the Cardiff Docks and other areas. It was the first time that I had had to deal directly with the treatment of mental patients, and for me it was an extremely interesting experience. I was also glad to get to know the nursing staff who were doing an excellent job there. However, it meant I had less time than I wanted for basic research. I was also short of the money that was needed for research. After making the necessary applications, I was glad to receive financial support from the Medical Research Council, and then a generous donation of £9000, a big sum in those days, from the Rockefeller Foundation. I was therefore able to proceed in appointing scientists to research posts. In due course I had appointed the biochemists Dawson, Hullin and Tyrrell with a physiologist Crossland, a histologist Jennett, a psychologist Boreham and physicist Cragg.

**Can I ask you who were the people you remember most from your Whitchurch days and what work were they doing?**

Well Wheatley and Hullin joined me in 1947 and we were studying the biochemical characteristics of subcellular brain organelles, and specially of isolated nuclei of the cerebral cortex. We were then joined by Dawson and Crossland who studied the biochemical changes produced by electrical stimulation and functional activity of the brain. In 1948 our Rockefeller grant enabled me to bring in Jennett, Boreham and Cragg. Boreham worked together with Kibbler in studying the relation of the alpha rhythm of the brain to psychomotor activity in response to auditory stimuli.

While most of our research was at first of a basic kind involving animal experiments, our EEG machine made it possible for us to engage also in clinical investigations involving patients. We were fortunate in getting a visit from Linford Rees and glad to cooperate with him in studies of the biochemical changes in the cerebrospinal fluid of patients after epileptic seizures and after ECT treatment. Another visiting research worker at that time was Francisco Grande, who was Head of the Department of Physiology at the Institute of Medical Research at Madrid. He joined us to learn the techniques that we were using in working with radioisotopes, and he carried out a piece of research on the effect of stimulation on the rate of incorporation of phosphate in mammalian nerves. He then left us to take up a Chair at the University of Zaragoza.

In 1949, the number working in the Unit had increased to 17 and we were joined by Ansell and Gaitonde, who took up work on the metabolism of the brain proteins, while Phyllis Croft started work on the effects of electroshock treatment. Other research workers who joined our Unit at Whitchurch include Dohmen from Cologne, who studied the changes in the brain phospholipids during functional activity, and Doris Clouet, from Nashville, USA, who measured the turnover rates of different brain proteins. Since our biochemical work was now beginning to be known elsewhere I could have brought in more biochemists but, remembering the principles I had seen to work so well in Hopkins' laboratory in Cambridge, when I was there in the 1930s, I brought in workers trained in other disciplines. McDermott, a physicist, came to study the different types of electrical activity in the brain, while Ingham, a psychologist, studied the mechanisms involved in suggestion and David, a histologist, looked at the reactions of nerve cells to stimulation.

In 1956 fighting was reported in the streets of Budapest and we read in the papers that Russian troops had fired on the crowds, so that 20,000 Hungarians had been killed. It was then that a young Hungarian biochemist, Robert Balazs, who had managed to escape, turned up in England and was looking for a job. Judging him to be person of ability I was glad to have the Rockefeller grants, which enabled me to offer him a post in our Unit. So he took up research with us on the metabolism of brain mitochondria. It was then while attending a Biochemical Congress in Vienna that a strongly-built man, in an apparent state of tension took me aside. He explained that he could be arrested at any time, since he was escaping from Czechoslovakia, where he had been doing research, but was having serious difficulties with the Soviet authorities. He desperately needed a post elsewhere. His name which he gave me, Dr Rudolph Vrba, I recognised as that of a scientist who had published papers in the Journal of Neurochemistry. I was glad to be able to help him by getting him a Rockefeller grant, and in due course he was getting down to research in our Unit.

**At the time that you organised the 1950 meeting, there also seems to have been a very active endocrine group in Bristol with Hemphill and Max Reiss. Can you give me some more feel about how you viewed what they were doing and whether you thought it was going to be important?**

I had no doubt about the importance of their work in Bristol. In fact I was very interested in them. Of course, from time to time, I called over and I was very well treated by them.

The work of Grey Walter especially interested me. He helped to bring into our lab EEG equipment which I used for studying patients in the wards. I was astonished that there was no electroencephalography carried out there at that time until I brought in this equipment. I then found that psychiatrists in Swansea and other parts of Wales were sending patients for me to examine their EEGs.

**Were there any other key people during the 1950s?**

There were a number of active workers in this country at that time including Philip Bradley, Joel Elkes, Archie Todrick, Harris, Eccles, Strom-Olsen and Weil Malherbe.

**Where did the idea for the Mental Health Foundation come from?**

Well, that was entirely my idea at the start. When I wanted to do research at Cardiff. I asked the Physician Superintendent how much money there was, and there was only a ridiculously small amount. He said only a few hundred pounds a year. Now, although I was fortunate in getting considerable support from the United States and from other sources, I realised then that there was no charity in this country making money available for mental health research. There were charities for animals and for cancer and other things like that, but not for mental health.

It was obvious to me that a charity was needed, and I discussed that with two or three people who agreed with me. Linford Rees agreed that a charity was really needed in the field

but how do you start a charity? I'd no experience of that and so I wrote to one or two old friends who might have financial information, particularly Ian Henderson, who I shared digs with in Oxford and who was in the Stock Exchange. He agreed to help me in starting a charity for mental health. How it started is in my little book Life in Research.

**You also began the Journal of Neurochemistry. Tell me why you felt such a journal was needed. Marthe Vogt had a part to play in that didn't she?**

Certainly, she came into it. At that time there was no neurochemical journal. I was approached by someone from the Pergamon Press so I contacted Marthe Vogt and we agreed as to the need; I then gave them the names of various Americans and others who might help as editors and we developed the idea of the journal in that way. The Americans were prepared to come in and help from their angle, while I was dealing with the actual production and dealing with Pergamon Press directly in determining how the journal should be run.

**Robert Maxwell was in charge of Pergamon then was quite a character to deal with, do you want to comment on that?**

Well, I saw him of course over the starting of the journal and met him on other occasions. It then happened that we rather fell out with him, because he reckoned he was running the journal and could do what he liked with it regardless of the wishes of the editors. Not only the pricing but the editorial arrangements and so on. The other editors who I brought in were very annoyed at that. We had an international symposium meeting on the continent, a meeting at which we were discussing various neurochemical matters and Maxwell decided to turn up at this meeting. As I was Secretary of the Society, I had to tell Maxwell that he was not invited to the meeting. He arrived in his yacht, and I had to be waiting for him on the bank to tell him that he couldn't come.

**What kind of man did you find him?**

Oh, I had great respect for him, because although he had shortcomings he was also an excellent person in many ways. That was my impression of Maxwell. He told us of the things he had done in the War, in the fighting. He got an MC. He had done much and he was also well qualified. He spoke fluent Russian, which was of real value in dealing with the Russian people. So although you could have disagreements with him you could also be on his side. Where the authors felt that he was being too authoritative in running the journal, it was there that our disagreement arose and I felt we had to fight him. We couldn't just let him do as he pleased with our journal. The editors had to decide and so I then brought together a group by bringing in the editors of other journals. Finally this group overcame him and he agreed to the things we wanted in the running of the Journal of Neurochemistry.

**This was the Scientific Publication Council. You were responsible for that**

I was, I started it. The main object was to fight Robert Maxwell and get our journal run in the way it should be run. But that applied not only to our journal. There were other journals run by other groups, where again the editors were having serious difficulties with the publishers over the running of their journals.

**Maxwell seems to have been fairly important also in that he had a great number of neuroscientific journals in Pergamon Press - the Journal of Psychiatric Research, Neuropharmacology and a few others**

He started several. I got him to start another journal, Neuroscience later. I found him an excellent person at his job. I remember he invited us to a dinner at The Savoy, Molly and me, and things like that. He was an all-round mixed character. You couldn't help liking him in many ways.

**How important do you think it was that English became the scientific language? I guess the fact that all these journals began in England helped that process**



Very much so. I was naturally in favour of that. There was opposition from the French who felt that French was a language that should become the international one but broadly speaking English was spreading, and I supported that and was very glad to do that. Recently I brought out a little book English Usage Guide to help people attending international meetings at which English is the language spoken.

**During the early 50s you visited the USA. Who were the people who most struck you over there? Who impressed you? Seymour Kety, Jordi Folch, Heinrich Waelsch?**

I went several times. I was invited to give papers and so on over in the States and I moved round and met a number of them but, in a sense, all these people impressed me, particularly Seymour Kety who I thought was doing a fine job. I thought they were doing excellent work over there and I was glad to co-operate.

**What was Heinrich Waelsch working on?**

Heinrich Waelsch was head of a big research laboratory at Columbia University, New York and he asked me to give a paper there on amino acid and protein metabolism in the brain, as that was a field in which he was working at that time. I was also invited to the Menninger Foundation and I was very impressed with Karl Menninger who invited me. Because this was essentially a psychoanalytical organization. It astonished me that, unlike the psychoanalysts in this country, they should invite a person from the opposite side, and he even offered me a post there. He tried to persuade me to take a post in the Menninger Foundation, but I preferred to keep my own post in this country. So that was the situation over that. But it was a very good experience over there.

**Where did the idea for IBRO come from?**

It was at an International Colloquium on the EEG in Moscow in 1958 that those who were present agreed on the need for international collaboration in brain research, and a group which included Herbert Jasper therefore sent to UNESCO the proposal to start IBRO. In due course, IBRO was registered as an independent organisation and with Herbert Jasper as Secretary General it did a fine job. Later, however, IBRO ran into difficulties when the support it had received from UNESCO was withdrawn and the Secretariat it had in UNESCO House was closed down. I then received a phone call from Montreal, when Herbert Jasper asked me if I would deal with the central administration of IBRO and set up a Secretariat in London. That was shortly after my retirement in 1972.

I felt there was still a real need for international co-operation in brain research, and the Institute of Biology generously allowed me to use a room in their London offices as the IBRO Secretariat. Soon I had found an able secretary, Bridget Robinson and, before long, as Secretary General at IBRO, I was travelling round organising meetings in different countries round the World. I also arranged the publication of a new journal IBRO News which I edited, so before long my work for IBRO became almost a full-time job.

**Let me change from people. What were the important techniques you used and when were they developed?**

We used the best techniques that were available at the time. I have mentioned our EEG machine which recorded on a graph the electrical activity of the brain. I was impressed by the splendid pictures of nerve cells recorded by the interference microscope used by David and Brown. We were also using high quality Geiger counters to determine minute amounts of radioactive elements in different tissues and to measure protein turnover in the brain.

**Your early work I would presume was shaped to some extent by the development of chromatography in Cambridge in the 1930s and subsequently by the development of the spectrofluorimeter. Am I wrong to place so much emphasis on techniques?**

No. You are right that the techniques we used played an important part in our work .

**Do you want to tell me something about why you moved from Whitchurch to Carshalton?**

Well, the reason was perfectly clear. At Whitchurch we had no co-operation at that time with the clinical workers there. I had a visit then from top people in the Medical Research Council, who very kindly said they would like to take over the Unit I had developed. I made it clear to them that what I wanted was to join clinical research with basic research, but that that was something I couldn't do at Whitchurch. So they said well you can go where you like. You can go anywhere in the country, just let us know where you want to go. So that was a great experience. I travelled round to Oxford, Cambridge and various other places and finally, seeing all the London patients in Epsom, I decided that a Unit near Epsom would be in the best interests of the kind of research I wanted to do.

There was a Unit then working at Carshalton doing toxicology, and as they had a big library I thought that if we could develop our Unit near there I would do so. So, I visited the place and found a stable there. The Medical Research Council then agreed with my proposal to convert this old stable building into laboratories, and that was precisely what they did. It took a little time, but soon they got horses out and cleared up the place. Then they put the benches into the Unit which became known as the Neuropsychiatric Research Unit at Carshalton. Then, when we were there, we developed part of our Unit in one of the Epsom hospitals. I tried different hospitals and finally we got into the West Park Hospital where I appointed Alec Coppen as a person who could take over on the clinical side of our work. That was in 1960.

**Who do you remember most from the Carshalton period and what were the principal lines of research there?**

We continued to develop the main lines of basic research that we had been doing at Whitchurch on the metabolic activity of the brain. But our clinical research ward at West Park Hospital made it possible for us to study the changes in patients with mental illnesses of different kinds. Coppen and Shaw started investigating the causes and treatment of depressive illness, using a recently developed multiple isotope technique, and it was a real joy for all of us when they were named as winners of the Anna Monica Prize for the outstanding work they had carried out. In due course, they started a lithium treatment centre, the first in this country, for patients with manic- depressive illness.

Others engaged in clinical research included Ricard, who studied the metabolic characteristics of groups of schizophrenics, Brenda Herzberg, who studied the mental symptoms associated with pre-menstrual tension, and Reynolds, who determined the vitamin deficiencies that arise in epileptics treated with certain drugs. A study of the effects of meningitis on the mental state of young children was carried out by our psychologist Maryse Metcalfe.

The main theme of our basic research was still the study of biochemical factors affecting the functional activity of the brain. Balazs was now studying the effect of thyroid deficiency and other factors on the enzymes concerned in the early development of the brain and, in collaboration with Thelma Julian, he was using an analogue computer to measure the different pathways of glucose oxidation in the brain. Gaitonde was studying the sulphur metabolism of the brain and collaborating with Gaull in studying the defective gene in patients suffering from homocystinuria. Vrba was investigating the effects of insulin on brain metabolism, while Brierley, Meldrum and Brown were working together on the effects of reduced blood pressure on the local electrical activity of the brain.

**How long were you at Carshalton before you retired?**

I was there for 12 years until I retired in 1972. By that time the number of permanent research scientists in the Unit had increased to 15, and we had eight visiting research workers, mainly from other countries. I was glad to hear Sir Harold Himsworth refer to our

Unit as 'a Mecca for scientists from overseas'.

**You've always been something of an enthusiast for getting people interested in research. The fact that you organised the symposia you did during the 50s and 60s was probably particularly important in the development of the field. Why do you suppose it was you, as opposed to other people, who felt it was important to get people together?**

That was my experience. I knew there was a big need for brain research in this field, which had been so neglected for so long. It was because for many years the mental patients had been stuck out in asylums away from the medical schools where research was carried out, so no research had been done. They had been simply neglected and I could see a big need for research. An example of the value of research is the condition known as GPI, which at the beginning of the century accounted for as many as 10% of all the patients admitted to the mental hospitals, but then latterly by the time I left you could hardly see a single patient suffering from GPI and that was all because of research. People didn't realise that that was the situation.

**Are there any other big breakthroughs that you think we've made? Schizophrenia has remained stubbornly resistant really hasn't it?**

Yes, but I think that Tim Crow and others have done excellent work in recognising the changes in the brains of schizophrenics and in realising that there are environmental as well as genetic factors involved in producing schizophrenic symptoms. The drugs that we now use help to get many schizophrenics out of hospital, so that they can now live in the community.

**Coming back to the point I was asking you about. Why do you suppose you were so keen to get people together to talk about research? I can see why you were keen for the research to be done, but so were very many other people in the field. You seem to have also been keen to bring people together in order to provide a cross-fertilisation of ideas**

I found that that was something of real value to people. There were informal meetings, sometimes in pubs and that sort of thing, that helped people to hear different viewpoints and different ideas. But one important thing in the Units I developed was to have regular afternoon tea sessions where I invited outsiders from different countries and from different parts to come in and talk about their ideas and their work. And gradually these ideas went round and helped people. They found out what they wanted to do, how they could do it, all that kind of thing. I felt it raised the standard of the work that was going on and it also developed a kind of family feeling, so that the members of the Unit were all ready to help each other. That was evident at the evening pub meetings at which Francisco Grande used to bring out and hand around a big box of cigars. Another thing that helped to bring people together was a 'lab scrap-book' which we kept in the library and which contained references to matters of common interest to those working in the Neuropsychiatric world, including one or two of a humorous kind. It was Hopkins at Cambridge who used to say 'knock their heads together'.

**You also seem to have been very keen to train people from other countries**

It was simply that they had heard about the work we were doing from our publications or from contacts and asked to come in. They got their grants from outside sources and asked if they could join us, and I was only too pleased.

**Of course, who wouldn't be. Can I ask you about your role in the development of the Brain Research Association?**

It was while attending an IBRO meeting in Paris that I noted that in the USA they had a local neuroscience association which was evidently doing well, and I felt that we should have a similar association in the UK. I therefore wrote with Donald MacKay to the other UK

members at IBRO asking if they agreed to our starting a Brain Research Association in our country. Most of the answers in favour, but some were against, so in order to reach a final decision I arranged a meeting in London, which all were invited to attend. At that meeting, I explained the general idea of an association that could arrange discussion meetings of the kind that we had in our own Unit and the establishment of the B.R.A. was agreed. In due course, local groups of the B.R.A. were set up in 16 different regions and the membership grew to more than 1000.

I think we should also recognise the contribution made by the World Health Organization (WHO) in helping to develop research in mental illness throughout the world. In the 1960s, I attended many meetings at Geneva of a Scientific Group they set up to collect information on mental disorders in different countries. In 1968, I served with Kety and Lebedev on the Secretariat, and the Director General agreed to our proposal that they should set up WHO Collaborative Centres in different countries for active collaboration in psychiatric research. It was at the Geneva meetings that I learned of the high mortality rates and ill health of the people in some third world countries, due mainly to the lack of skilled scientists and technicians, who could apply the remedies required. In many countries, there was little or no science teaching in the village schools and strong opposition to women entering the scientific field. Hoping it would raise the general standard of health, I therefore invited a group of women scientists in different countries to send an account of their experiences for publication in a little book. The accounts they gave of the difficulties they had overcome were impressive, and I hoped the book *Women Scientists The Road to Liberation* would encourage more women in all countries to take up the study of science and make a scientific career. It was encouraging then when one of the contributors to the book, Rita Levi-Montalcini, was rewarded for her research by being made a Nobel Laureate.