

8 George Ashcroft

The receptor enters psychiatry (1)

I came up to Edinburgh in 1956, having just come out of the army. I came up to do the membership course in medicine. Whilst I was up here, there was a job advertised in psychiatry and, as I'd always intended going into psychiatry eventually, I went in slightly earlier than I'd intended. I came at an exciting time because reserpine was already in use, chlorpromazine was just coming into use and the monoamine oxidase inhibitors and Tofranil followed in the next year or so. So, it was an exciting time. I became interested in why reserpine produced depression and why the antidepressant drugs worked.

You were saying to me before that reserpine produced fairly dramatic responses in some cases.

Yes. I think it produced recovery in some cases, which makes me doubt the whole of Crow's theory of schizophrenia because, with this theory, you couldn't produce recovery in a person with schizophrenia. I've always doubted this. I've always thought that schizophrenia was potentially recoverable.

In the patients who responded in a way they didn't to chlorpromazine, was this response anything like the response people talk about these days to clozapine?

Yes. Probably better. I saw people get well in a way that I've never seen anybody with that sort of severe schizophrenia get better on any other drug. They'd been ill for years and I saw a number of them get better and go home to their families. It didn't do it for many people, but when it did it was very striking. I wonder what happened to them? It should be possible to get the notes out of the records department.

Why did chlorpromazine take so long to come through? It was licensed in 1954.

That's right. I started in Edinburgh on the 1st January 1957. It was just reaching Edinburgh then, but we were still using reserpine because they knew it. It was about 9 months later that chlorpromazine really began to take over. Reserpine was an interesting drug, but it also produced depression in some patients.

Was this real depression?

I think so. I know that Jenner's group eventually suggested that it didn't produce depression and there was just an association between hypertension and

190 The Psychopharmacologists III

depression; well, I think that's probably wrong. You saw patients with schizophrenia treated with reserpine develop very severe depressive symptoms and become suicidal.

It also produced akathisia, didn't it, which could potentially make you suicidal?

It gives very severe parkinsonism. I don't know that it produces akathisia as much as haloperidol, for instance. It was very toxic. We had two deaths, which were due to a myocardial fibrosis, which was probably because it depleted the heart of noradrenaline and affected its metabolism. But we were giving up to 15 mg a day. Because of its toxicity, when chlorpromazine came in, we largely switched to chlorpromazine for schizophrenia.

Did the idea that it depleted 5HT lead into your early work on 5HT and depression?

Yes. I'd read Brodie's hypotheses about this. I was lucky because in Edinburgh there was a group of people who was working on cerebral monoamines. Martha Vogt had discovered noradrenaline in Edinburgh. Tom Crawford and Gaddum had discovered 5HT in brain in Edinburgh.

At the time they found 5HT in brain, what you read is that they weren't sure if it just leached in from the blood.

Crawford was sure. I mean, he did it so carefully that he would have allowed for the amount of blood in the brain. He was probably the most careful biochemist working in the field that I've ever come across. He wouldn't let you claim anything that he hadn't checked about a dozen times. A very obsessional man, but a very good scientist.

What was his background?

He was a chemist initially, then he became a biochemist. He worked during the war on British Anti-Lewisite, the chelating agent, and then Gaddum persuaded him to start to work on amines and he was really the person who did all the work on noradrenaline for Martha Vogt. And he discovered substance P in the brain. I was doing psychiatry at the time and my boss, Elizabeth Robinson, knew Martha Vogt. Kennedy was the professor of psychiatry then, but Elizabeth Robinson and Kennedy didn't speak to each other, so I wasn't allowed time to do the DPM course, even though I worked in the hospital where it was held. I was allowed time instead to go and work in the neurology unit and in the pharmacology department. These days, I would have never learnt anything whatsoever about 5HT because I wouldn't have been allowed to do this. I'd have been made to do the course. So, in fact, I got my membership in medicine, with neurology as the main subject, before I sat any DPM subjects, 3 or 4 years later. It was a very idiosyncratic sort of development.

I initially tried to measure 5HT in the cerebrospinal fluid (CSF). I had the idea that you might get a direct measure of what was going on in the brain by looking at the CSF. So, I spent about 6 months measuring 5HT in the CSF using bioassay. You had to wait 4 minutes between each drop that you put on

Robertson

the rat uterus, so, being a very impatient person, this was good for my soul. It taught me to be patient doing work. Then there was a chap there, Dennis Sharman, who developed a technique for measuring 5HIAA and from then the work took off. We measured 5HIAA in CSF and showed that 5HIAA was a better measure of turnover than 5HT in brain. Later on, we looked at 5HIAA in depression and showed that it was low in the CSF in depression.

How common at the time would it have been to take CSF from patients?

Well, remember that there had already been studies on brain using air encephalography and quite a few psychiatric patients went for that and you could get CSF while that was being done. We did CSF as a routine. My boss was interested in presenile dementia and you did quite a lot of CSF studies in those cases. Remember, also, that I was attached to a neurology unit, where it was a common thing to do. So it may have not been common as a routine, but we explained to patients why we wanted to do it and they were happy. I got quite good at doing lumbar punctures. I even employed a technique of using a double needle to try to avoid post-lumbar puncture headache. We also looked at CSF that we obtained from neurology and neurosurgery units, which I developed a link with. We found that there was a gradient of levels in the amine metabolites, with the highest levels in the ventricles, lower levels in the basal cisterna and lower levels still in lumbar space. I spent about 2 years trying to find out why that was, and discovered the probenecid blocking effect on CSF in animals and the fact that there was a transport mechanism for 5HIAA. In humans, it appeared to be in the choroid plexus of the fourth ventricle. We looked at the physiology of that in the same way that you would at kidney. We did clearance studies and tidied it all up. In the end, we came to the conclusion that lumbar CSF was like looking down the wrong end of a telescope. You were very far from the main event, but it may still give you some sort of indication. At that point I had a fairly mechanistic view of what depression was all about. I thought there was probably some genetic abnormality in the production of 5HT.

At that time, when you talked to people at a party or whatever, and they asked what you were doing and you'd say, 'I look at things like 5HT in the brain', would they have thought that this was ungodly in a sense? Such a mechanistic view of how the mind works.

Not in Edinburgh, because Kennedy, the professor, for example, had a very organic view of psychiatry. And my boss had a very organic view of psychiatry. There was an organic or biological group in Edinburgh. Sir David Henderson was only just leaving the place when I came and he'd had a very open, very eclectic view of psychiatry. You could argue in Edinburgh. It was good to be here. In the big ward rounds, you could say what you felt and you wouldn't get shot down or, if you did get shot down, you were allowed to retaliate. It was very healthy. I found it different elsewhere. You might be regarded as aggressive if you dared to speak out. Here, you were regarded as stupid if you didn't. It was a good place to be and, of course, it was a very active pharmacology department. Gaddum had only just left and gone down to Cambridge.

192 The Psychopharmacologists III

What was his impact and what was the effect of his leaving?

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His impact was to look for all these active substances in the body. In other words, it was a sort of endopharmacology. He encouraged people to look at the brain and at the gut. He was also a bloke who encouraged people to think of ideas. It didn't have an enormous impact when he left because, interestingly, he hadn't done the work. The people who were left behind were the people who had done the work and you still had Crawford, Adam, Vogt, Barlow. There was an interesting chap called Steyenson who was a receptor expert. Every 4 or 5 years he would write a paper on receptors that destroyed everything that was known at that time and then he played tennis for another 4 years, basically, and thought. Then he would do another paper. All the background work on producing analogues and testing relative efficacy was done by Dick Barlow, who was a chemist. There was a lot of debate. I was the only medic wandering about the place at that time and they were actually quite keen to apply what they were doing to something to do more directly with medicine. It was a good place to be and I was just lucky.

When the idea of 5HT in the brain was first mooted, there must have surely been some question about whether it was a neurotransmitter in the brain. The fact that it was a neurotransmitter in the periphery didn't mean it was one in the brain. Where these ideas still there?

Yes, they were. And eventually people like Ginsberg, a neurophysiologist, came into the department, probably as a result of these questions. John Kelly, the current professor of pharmacology here, did his PhD with a neurophysiologist in the next lab to me. Neurophysiology came in and brought with it the functional side of things. I worked on CSF, looking at mechanisms for transport, how it got into the CSF, and so on. We found HVA in CSF one evening in our lab over the infirmary. To my horror, when I arrived home at about 11.30 that night, there were a set of cars outside my house – twenty. I'd forgotten we were having a party. My wife had been trying to get me but I was in the wrong lab. That was the night we found HVA in CSF. It was a very exciting time. It wasn't unusual to work until 2:00 and 3:00 in the morning.

Then, in animals, we did loading with the 5HT precursor tryptophan, to see if we could get a measure of the maximal synthetic ability for 5HT. We wanted to see if you could push the system, overload it and show there was a maximum. We showed it in dogs and then we thought right, we could do the same in humans. We tried it in neurological patients and found you could give a load of tryptophan and 5HT would rise in the CSF. Then we did it in a range of psychiatric patients and showed, to our horror, that there was no failure of production of 5HT in depression. People with depression or recovered depressives had exactly the same maximal synthetic capacity as people without depression. That, together with a few other facts, led us to think that if 5HT is involved – or if any of these transmitters are involved, because the same thing probably applies to other transmitters – then there must be more than one variable at the receptor. There must be more than just the release of the transmitter.

The receptor enters psychiatry (1) 193

Before we move on to the receptor developments, how was your early 1959 paper saying that there is low CSF 5HTA in people who were depressed received? This is really one of the earliest claims in the area.

There was another one just about the same time by a chap called Roos in Sweden and we met and discussed it. I think the paper was well received. I am not a great meeting attender and I didn't go and push it. Once I've found something, I'm not really worried whether anybody else knows. I'll publish it, but I get satisfaction out of finding the answers not talking about them – the eureka experience. It's happened about three times.

The paper meant I got scholarships. I got a medical Research Council (MRC) fellowship so, instead of doing the work part time, I could do it full time. I subsequently got a Mental Health Foundation scholarship. They enabled me to break off and do lab work full time for about 3 years, and then I went back and did both clinical and lab work. There was a lot of real work to do in a lab in those days. We used to have to wash all our equipment forty times – there were no dishwashers or anything like that. We didn't throw out test tubes. We had to steep them in chromic acid, wash them twenty times in tap water and then ten times in distilled water. This was because the only way you can measure the small amounts of a substance spectrofluorimetrically is by having low blank measures. If your blank measurements were high, you couldn't measure them and so you had to do all the things you could to keep those down – using desperately clean glass wear was the main way you did it.

Did the spectrophotofluorimeter make a big difference when it came around?

Yes, because you couldn't measure metabolites by biological methods. All the methods that had been used to measure the original amines in the first place were biological methods. Later on you had HPLC, which gave you a lot better resolution.

This is the age-old question then – how much does the progress in the field depend on the technology as opposed to the great ideas?

A lot. Dennis Sharman had one of the first fluorimeters of this type imported from the USA, the one that you could scan input and output wavelengths with. By doing that, you could get very specific measurements of substances. It was not as sensitive as subsequent HPLC, but you could measure metabolites and a range of substances in nanogram amounts. We would use paper chromatography to identify compounds. Our paper chromatographic technique took about 6 hours. The only way you could live a reasonable life was to go in and set it going in the middle of the night. So we had an alarm clock with a lever on it that turned a tap on a separating funnel, which let a solvent into this tank in the middle of the night. Occasionally, this would fail and you'd go in the next morning to a mess. To try to avoid oxidation of these small amounts, we ran the chromatograms in a nitrogen atmosphere. It was quite an elaborate procedure. We actually showed that the American work on tryptamine was all wrong, because their technique hadn't separated it from other compounds.

194 The Psychopharmacologists III

Tom Crawford was hovering over this the whole time. He was the one who provided the carefully validated techniques that I would then apply to ideas. It was a good combination and we worked very closely together. I can remember the first paper we ever wrote together. We got to twenty-odd drafts; eventually I sent it off. I went in one morning and said, 'I'm sorry, I can't bring it back for any more drafts, I've sent it off. I can't face it'. He didn't annoy me, though, in the way obsessional people usually do; I'm not very tolerant, but there was something about him that made you know he was doing it for the best, and it was good for me. So we got on very well, but he would make you work until 1:00 or 2:00 in the morning to complete an experiment.

When did Don Eccleston join in?

I can't remember the year, but he came from Aberdeen. He was looking for somewhere to do a PhD. He had looked at one or two places and he came down to see our laboratory and he decided that that's where he wanted to be. He was mainly looking for tryptamine, but he also worked on the 5HT work that we'd already started. He also did clinical work and eventually we developed the clinical side of the Brain Metabolism Unit.

Okay, now you're in the mid-1960s, beginning to say that the 5HIAA story is more complex. When you gave the tryptophan loading to people, you weren't able to show that people who were depressed who were any different.

What we believed was that 5HIAA levels were probably a measure of functional activity of the system and not a cause. It could just as well have been that people with depression had low activity in their system and that 5HIAA was mirroring that and then, when they got better, it didn't necessarily go up. Now that was slightly worrying. We had to say, 'Well, it doesn't go up and yet we are saying that the overall activity of the system beyond that is going up or changing. There must then be another variable'. If we were going to try to maintain this theory, we had to introduce another variable, and the other variable which we found would explain most of the facts we had at that time was a change in receptor sensitivity.

When did you begin to think that way? The revised receptor version of the monoamine theories came out in 1972. But how long before the article were you thinking this way?

I think about 2 years. Remember, we were in a department of pharmacology. My university post at that time was Honorary Senior Lecturer in Pharmacology, not in psychiatry. And we were teaching there – we had to teach for our supper. We were aware of denervation supersensitivity in cholinergic systems and so the idea that we could get a change in receptor sensitivity was already there in pharmacology. I don't think anybody at that time had applied it to brain, but why not? Being in a pharmacology department was also good in that you could sign your ideas off with scientists. That's the way we started to think about it. Then I wrote that paper and stuck everybody's name on it. The way I tended to write papers was to sit down and write them in one day. I can't

The receptor enters psychiatry (1) 195

do it in little bits and join them together. I'll edit it and refine it, but I'll write it all in one go. So, I wrote the whole of that paper in one go.

What did the receptor look like at the time? What did you think you were dealing with? Was it a lump of protein that was going to take a while to change and this might explain the slow response of the antidepressants etc.?

That's what people said. I never believed that. I still don't. I wasn't sure how long it took for a receptor to change. I thought that what was happening was that a system was trying to return its activity back within the normal range of variation. I actually wrote a paper about 1960 putting forward this idea – that there was a norm in these systems. So I thought that changes in output and changes in receptor sensitivity were designed to try to return the system to the norm, and what happened in depression and mania was it didn't bounce back. We did put forward the idea, which has never been taken up, that there was both a low-output depression and a low-sensitivity depression. We put forward the idea that the sensitivity depression was the bipolar one, with mania being the high-sensitivity pole. Nobody has ever taken this up. There may even be a high output mania as well, and that may be what you get with amphetamines. I still think there might be something in this.

Just to come back to historical context, receptors hadn't been isolated at this point – you were still talking about a somewhat mythical beast, even though you were in a pharmacology department.

Yes, you were. Although we were talking to people like Stevenson and Barlow, who believed in their existence and believed that, by testing them out with partial agonists and antagonists, with a range of compounds, you could identify the characteristics of the receptor.

All of that goes back to A.J. Clark, who originated receptor theory and who, of course, was also from Edinburgh. Was his influence around then still – a ghost hovering in the background?

No, but in 1960 I went down to Cambridge, following Martha Vogt, to finish work that we were doing with Dennis Sharman. And where did I end up living. In Fulbourn Hospital with David Clark, A.J. Clark's son. My boss, who knew him very well, wrote to him and asked if there was any chance of me staying in his hospital. So I sang for my supper. I lived in Fulbourn and worked at Babraham in animal physiology.

Father and son were very different then: one was the archetypal pharmacologist and the other was not so much an antipharmacologist but very much the social psychiatrist.

Yes, but I presume the two had one thing in common – enormous drive, not in the same direction, but they both had tremendous drive. David Clark carried through what he did with virtually no psychiatrists to help him, possibly, in fact, because he didn't have any to help him.

196 The Psychopharmacologists III

Fascinating. Okay, so we're back now to receptors. You produced your article and within months receptors were radiolabelled, making your article highly topical.

At that time, I wanted to radiolabel them and I wanted to work with the people at the Western General who had a cyclotron. I produced for the MRC a programme that would have involved us developing what was virtually positron emission tomography (PET). But the MRC procrastinated and messed about, as was their wont, and by that time I was getting disillusioned with them and having major arguments with them and, in fact, meeting with some ~~crookery from them~~. On one of their visits, a neuropathologist came to see what we were doing. At the time, we were also working on Alzheimer's disease and appeared to have found a cholinergic deficit. He came and told us to stop this work and to stop work on the aluminium model in animals. I said we weren't stopping it. A fortnight later, he was on the radio saying how they were developing the aluminium model in his unit. We also found out that they were working on the cholinergic system.

That's serious trickery.

Very serious, yes. We wrote a paper and sent it in. My name was on it and it got rejected by *Nature*. Now, this was ridiculous because this was a very original finding and it was the first time anybody had said there was a cholinergic deficit in Alzheimer's, so I rang the editor of the *Lancet* and said, 'I think we're being done here'. He said, 'Send it to me and if it's what you say I'll referee it and I'll give you a year's jump in publication'. I felt a bit disgusted so I took my name off the paper because I didn't think I should benefit from this sharp practice personally. So we got our paper on the cholinergic deficit published in 1976 and the others didn't get it until 1977.

The whole thing disillusioned me. It was one of the reasons I left the MRC. The other reason was that I felt a lot of the studies now had to be done in a different way. We should move away from animal work almost completely and work on humans, but they were virtually saying 'You are the animal people, you keep doing that'. So, to get freedom to work on humans, I moved up to Aberdeen.

Your approach towards all these things seems very honourable, but over in the USA it would have been par for the course to play the game more vigorously.

Yes. The Swedes were like the Americans, too. I never had trouble thinking of another idea. So it never worried me. I didn't see the point of getting all tied up in whether this was my idea or their idea; I still don't see the point in it.

The ethos has changed. Science was a very gentlemanly thing to some extent. 'Yes, there was competition between people, but it's become a much more self-serving business now.

Yes and I think it loses people who would otherwise make a contribution. How many major contributions have been made in the last 10 years in the biological field? I can't think of one really fundamental one. I think also that you need people coming in from the clinical field. There is another problem now and

difficulties in my dealings with them

scientist

ADD - we wrote to them suggesting that we should submit the findings in Alzheimer's together but did not receive a reply.

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The receptor enters psychiatry (1) 197

that's that the scientific field is so complex that it's very difficult for a clinician to grasp the issues.

Psychiatry is actually very complex as well.

Yes, you still need people to do both things. Just before I came up to Aberdeen, a fellow called Roger Makendula, who became a professor of psychiatry in Ifa in Northern Nigeria, and myself were toying with the idea that really the parallel to mood in humans was exploratory behaviour in animals. We did a lot of animal work showing which systems were involved in exploratory behaviour in animals. And, based on that, we launched a hypothesis on the way in which depression, mania and certain types of anxiety were related to changes in exploratory behaviour. I still believe that the most fundamental change in a mood disorder involves exploratory activity and thinking and that mood is just a label for this.

Quite a few people hold this idea, that there is no such thing as mood in one sense, that activity is actually the core variable.

And the type of activity. You've got exploratory thinking and you've got stereotyped thinking and we looked at which systems were involved in each of these. You could argue, for instance, that the depression you get with panic is really because panic anxiety inhibits exploration. People who are experiencing a panic attack don't explore and then they become depressed. I wanted to go along these lines and look at this in both animals and humans and the MRC wouldn't let me. They said, 'No, you're a CSF man', so I said 'Fine, I'll go and do it somewhere else then'.

Also, when I got to Aberdeen, the professor of physics then, Mallard, came across to me and said 'Look, I'll show you how to image a rabbits brain'. He took me to his lab and he showed me nuclear magnetic resonance imaging (NMR) in rabbits: He had developed it in parallel with the people in Nottingham. He asked me what we would do with it if we could do it in humans. I said we'd start by imaging people with dementia, and all the work that John Besson did on dementia stemmed from this 'What would you do with it?'. So we got into that and then later Adel Mousawi did PET imaging.

Can I pick up another angle on the receptor story, which links back to the reserpine story? reserpine and the 5HIAA work is all presynaptic. Does the receptor open up the area of postsynaptic changes? Were you thinking much about those issues at all?

Yes. If you look at some of the work that Donald Eccleston did, he actually imported a neurophysiologist from Aberdeen, Gordon Arbuthnot, who had worked on lesioning and sensitivity changes with Ungerstedt in Sweden. We imported him with the idea of introducing neurophysiology and looking at presynaptic and postsynaptic changes.

Was there any thinking that presynaptic and postsynaptic changes might link up to different kinds of behaviour? Learning theorists might have linked presynaptic changes with behaviour that can be conditioned.

198 The Psychopharmacologists III

No. I became more interested in the systems and this is where the ideas about exploratory behaviour came in – it was what was happening in the system. I thought we had got obsessed with the synapse and lost the idea of what different systems did. I felt that clinicians can tell you more about what's happening at the systems level and that the basic scientists should be listening to them.

So, paradoxically, you were at the forefront of what was happening actually in the synapse, but conceptually you were almost moving in the opposite direction. Were you aware of people like Tom Ban in the USA who were quite excited by the receptor hypothesis because, up till then, the focus had been presynaptic and this fits in with learning theory and conditioned and unconditioned stimuli, but the postsynaptic receptor opened up the notion of a lesion?

Yes, well, I was in a way giving up the idea of a lesion. I was going the opposite way. I was saying most depression is nothing to do with a lesion.

I can see that, but the oddity is that you were changing just at the time when the Holy Grail of a lesion comes into view.

Yes. I was aware later that some of the things that we'd talked about – changing receptor sensitivity – could have been due to autoreceptors turning off, so the system left room for a lot of other control mechanisms to come in. But I thought very few cases of depression were due to a lesion.

The work you'd done laid the path open, however, for the idea of a lesion, which appeared with Fridolin Sulser's beta adrenoceptor downregulation hypothesis. This is where all the antidepressants worked regardless of what else they worked on. Did you ever meet the man and what was your reaction to all this?

No, never. But I obviously knew what they were saying. By then I'd lost the idea that anybody was going to find the Holy Grail – one cause of mood disorders. I still believe that perhaps bipolar illness has some sort of lesion in terms of postsynaptic receptor sensitivity, and we said that was probably a failure to be able to readjust sensitivity. But I didn't believe there would be any specific lesion for most cases of depression. And to prove that, I can tell you, we took on Ivy Blackburn at that time and sent her off to Aaron Beck to learn cognitive therapy to try to broaden our view of depression, to bring back new ideas on how you can go into depression from a psychological point of view. I believed a lot of the biochemical changes had been precipitated psychologically, or at least you could get stuck in depression. I thought it was interesting to try to find out why you got stuck and why you couldn't get out. I actually still believe that many antidepressant drugs, from a functional point of view, restore the ability to explore and I think the delay in recovering from the depression is the time it takes to develop exploratory behaviour when you've been deprived of it. I think you're locked in to not exploring and you've got to start again, and if that doesn't take 3 weeks what will? I didn't believe there was a biochemical reason for it taking 3 weeks. I believe there's a behavioural reason for that – exploring

The receptor enters psychiatry (1) 199

outside your little burrow takes a bit longer than 5 minutes. Initially, you'll be defeated and go back in, and it probably takes 3 weeks to be able to re-explore. So, it's an interaction between biology and psychology.

But then there's a group of people that you worked on here in Edinburgh, which is the treatment-resistant group: you add in a little dose of tryptophan and you seemed to have flipped a switch almost – this looks very biological.

Once you've stopped exploration, it's very difficult to re-establish it. Now, if these drugs re-establish the ability to explore, then you may need to give the systems a real kick to restore their ability to deliver this sort of behaviour.

You say you didn't go to meetings much. Did you go to any?

No. I went to some small meetings. I went to a lot of Pharmacology Society meetings. I went to some meetings on depression run by the college.

What would people in the Royal College of Psychiatrists have made of this stuff in the 1960s? How many people would have thought the same way as you? Alec Jenner, Alec Coppen, Herman van Praag and a few other people, but how many?

Yes, and there were a few foreign people. We were going a long time before Alec Coppen in this area. He made some contributions, but it was as much in terms of raising the profile of the area. I read van Praag's work, but we actually had already done the probenecid work he later tried. We couldn't make sense of it so we never published it. I've still got it somewhere. I was the first person to take probenecid. I did this with tryptophan as well. When we were going to give tryptophan, I took 2 g of it every hour for 24 hours to see what would happen. It gave me an attack of migraine, but I think that was just because I never got any sleep. I did the same thing with probenecid. I took large doses of it to see what a patient would tolerate. That made me just feel very sick. I've taken various things to test them out on myself first. I took bromocriptine once. I felt very strange after taking it – derealized. We were going to give that because we had this idea that a dopamine agonist might stop mania.

Stop mania? Now that's creative.

We actually tried it and there's a little paper somewhere with amphetamine. It works, you can stop mania with amphetamine. Not reliably, but in some patients you appear to switch them off.

Is there any way of knowing who it would work for?

No. At that point, I thought a steady stimulation of the receptors if they were hypersensitive might switch off the sensitivity. I now believe it acts by switching off the neurone via autoreceptors. So, that was another idea. I don't have a problem with ideas.

On the map, Aberdeen looks remote from everywhere else, but it has quite a pedigree in terms of people like Hughes and Kosterlitz being there, the development of NMR etc. You didn't regret moving?

200 The Psychopharmacologists III

Oh no, I spent 20 years in Aberdeen after leaving the MRC Brain Metabolism Unit and was able to continue what I've always considered to be the most important part of our activities, which was clinical work, with research and teaching being carried out in parallel. During the last 20 years, I was pleased to see the development of young 'biological' psychiatrists in Aberdeen who have gone on to senior positions – John Besson in London, Klaus Ebmeier, who is professor in Edinburgh, Ian Reed and Keith Matthews, who are both professors in Dundee, and Adel Mousawi, who is now in London.

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