PERSONALITY, DISEASE & PSYCHOPHARMACOLOGY
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I often ask people why they went into psychiatry but in your case I wonder would it have been possible not to have gone into it - there's a certain history in the family isn't there?

Of course, my father was a psychiatrist. He had a brother who also practiced psychiatry. My mother has a brother who practices psychiatry and I have two cousins who are also psychiatrists. Furthermore, I am the eldest of 12 brothers and sisters, of whom 6 are physicians and of those 4 are psychiatrists. I have a sister who is a psychologist and 2 daughters in the medical field, so it seems like a genetic disease in my family. There are other families like this. There is a Spanish family of physicians in the Guinness Book of Records because for more than a hundred years there has been a physician with the same name in succeeding generations.

Extraordinary. Is there a reason why this should happen more in Spain?

I have looked with my students at the question of why somebody becomes a doctor. Now it's more difficult to say because we have examinations which limit the entrance into medical schools so it means that you are not as free to choose as we were in the past. In the past, you freely decided whatever you wanted to do and usually physicians in Spain came from families where a lot of people were either physicians or teachers in schools or Professors in the Universities - professions devoted to the service to people. So I think that this was something that you saw at home when you were young. Then our families have stronger links than in other parts of Europe - we live with our families a longer time than the UK for instance and this also plays a role.

So when did you go into medicine?

I went into medicine in 1957. But I was not so much interested in psychiatry in the beginning. I was more interested in basic research. I think that is something which every physician has gone through - the possibility of fascinating research in biological science. Before I went to medical school, in fact I thought about doing physics but it was not the right choice in a country like Spain. I also thought about archeology; I am a failed Egyptologist like many people in this world. Then suddenly I was fascinated by the CNS and I started neurology but I very quickly jumped to psychiatry.

How did the field look then?

It looked very complicated. I finished my studies in 1965. I was fortunate in one sense which is I had very extraordinary teachers in the medical school. At this time academic careers in Spain ended in Madrid. Every good professor had gone to one or two other universities and then ended his or her life in Madrid. So in Madrid we had the top level professors in the country. It was a generation of physicians who had gone through the Civil War, had been characterised by their endurance and by big efforts to renew their own speciality. So although we were very large groups of students, even if the contact with the professor was not very intense, the spectacle of such a group of people was enough to give a big impact on your self. I was glad of that. When I finished I went to Germany and there I was happy to find that my training has been as good as what you would expect from a country that was much more developed in this sense, as Germany was at these times. This was especially so on the theoretical rather than the practical aspect but if you wanted you could find time to develop practical skills in the hospitals with patients.

What was the primary orientation at the time in Spanish psychiatry. The European countries tend to split between those who were psychodynamically oriented and those that were more biologically oriented. Spain is interesting in that you have always had a tradition of biological research from Cajal and people like that...

Well in medical school we had two disciplines related to psychiatry. One was medical psychology which was taught in the pre-clinical years, as a basic science for medicine, and then psychiatry, as the specialty of psychiatry for all physicians. There was a great impact, I would say, from humanistic medicine, more than biological psychiatry. Most of the Professors of Psychiatry in this field at the time had had some training in Germany and were very much influenced by the German anthropological psychiatry - phenomenologically oriented and related to existential philosophy. This gave a very strong philosophical background for the speciality. This was seen as the goal of the training. It was very much linked to clinical activities and was quite a way from any reductionistic perspective be it purely psychodynamic or purely biological.

Ramon-y-Cajal was not a psychiatrist, he was a prominent neuroscientist. He never showed any interest in psychiatry. In his memoirs, Kraepelin tells about a trip to Spain, where he wanted to meet Ramon-y-Cajal. He mentiones that he was astonished by the ignorance Ramon-y-Cajal had of the developments in psychiatry in central Europe - he was not interested at all. He was primarily interested in neuroscience and histological research. He became a model for a generation of Spanish physicians in the sense that he was the scientist who brought science into Spanish medicine or even more into Spanish culture but he did not have much direct impact on psychiatry.

I'm Irish and coming from a Catholic background, there was a certain feeling in the 1960s that brain chemicals were not something that people really wanted to think about closely. The fact that the brain might be just a bunch of chemicals didn't seem to fit very well with a spiritual view of man. Did that apply at all to Spain?

Not in Spain. No. My family has a strong Catholic background, actually my father gave advice to the Holy See on issues of marriage annulment, where he took a very liberal view, and birth control, where his view was more traditional and both he and I have written on the interface between religion and psychopathology.

But the strong clinical background I described led some people in Spain, especially my father who started a very prominent school of thought, in the late 40s, to the notion that neurotic disorders were not of psychodynamic origin - that psycho-analysis could not explain neurotic disorders. If dynamic factors are not the explanation, some biological background must be involved. At first he thought it was only some of the neurotic disorders that this applied to but his research led him eventually to say that in every neurotic disorder there is a biological element, which can be treated with psychotropic drugs. So he tried drugs and other kinds of biological treatments, such as sleep, ECT, and a minor form of ECT - acetycholine shocks which were used by Fiambertti in Italy to treat depression. This was a mild form of shock where the patient did not lose consciousness. It worked. Then when psychotropic drugs became available, especially the tricyclic antidepressants and MAO inhibitors, he started using them and

these, in a sense, confirmed his ideas that some biological element was present and that this biological element could be treated.

How acceptable would that have been generally in Spain, at that time.
In general it became very widely accepted. But you have to add in another element, at this time - the late 60s, which is that social psychiatry, political psychiatry, anti-psychiatry in Spain was also linked with the last years of the period of Franco's regime. This led to struggles in psychiatry, which were very difficult, in the sense that people in academia were seen often as people who had some kind of commitment with Franco's regime. It was not usually like that - in the case of my father, he was deported once because of some writings against Franco after the War. I think the university was quite independant from the influence of the regime - I think this was because Franco never thought that the university was a danger. Intellectual life was really unimportant for a Big General.

Perhaps he was right.
Yes it's peanuts - these people can speak and write but real power is something different. Nevertheless, a group of psychiatrists were not very happy with the regime and they politicized very much the discipline. This was in the period of anti-psychiatry and it led to very strong commitments and an important struggle, as happened in other countries. This was when biological psychiatry was born, as a reaction against political anti-psychiatry, in many countries.

In a place like Holland, someone like Herman van Praag, had to have a police escort because there was a feeling that what he was doing was in league with Satan. This was not Christian.
This never happened in Spain. We were not, I was going to say so violent - except when we go to Civil War - but I think it was not this kind of problem. There were struggles in the media, in congresses, in meetings and in scientific journals. There was a lot of lobbying but it never became confrontational in the way it did here in Holland. Nobody lost his or her job, because of those kinds of things.

In the late 60s, I was planning a double-blind comparative study on intravenous nialamide, an MAOI, with placebo or tryptophan. In order to test its tolerability we did a few cases. The first one was a lady from Seville who had been depressed for 11 years. The third day of treatment with 500 mgs of nialamide and 6 grs of tryptophan, she came to my office requesting to be discharged as she had no symptoms. She stayed four more days. She was discharged and the following day she phoned to tell that on a precise spot on the train back to Seville, the symptoms had reappeared in full severity. I told her to come back which she did. I went through the treatment and I saw that for the last two days tryptophan had not been given to her because, being prepared in small amounts by the hospital pharmacist it was reserved for patients who might need it more.

We discussed the case at the big weekly round. At the time the antipsychiatric atmosphere was intense and the majority stressed the influence of psychogenic factors and the fact of relapsing while she was going back to a home with many difficulties. In spite of all this, I decided to go back to the full treatment and see what happened. The third day came with no change - a difficult day for those of us who believed in biological

psychiatry and serotonin but fortunately the day after the patient came to say that she was again relieved. She was discharged with nialamide and tryptophan and was followed up for three years with no reappearance of the symptoms.

You began to practice clinically in the mid 1960s. Fairly early on you were involved in one of the developments, which have been seminal really - the work with Clomipramine and OCD. How did you come to that?
This was following very much in my father's thoughts on biological treatment for neurotic disorders. This meant that every new biological treatment was tried in not only depression or whatever but also in other disorders. I had heard at the time that clomipramine could be used intravenously. Now, we had in our clinic, very severe cases from all over the country and some from abroad. I told my father that a man called Sigwald in France had been giving clomipramine intravenously and that we should use it for our severe patients and for other patients and so we started with this. Very soon we saw that in obsessive patients it worked and people started to get better. Not in the sense that the obsessions disappeared but the patient became more able to resist the obsessions.

This effect of clomipramine is very different to its effect in depression and that is why we thought it was something specific. Just as any other antidepressant, clomipramine washes away the symptoms of depression as an analgesic produces relief of pain. But in obsessive patients, it is different because the obsessions may remain very long, while the patient gains control over them. The first patient was a young man who would not touch something that had been touched by another human being. He had long-standing washing routines. One day after hearing from him that his condition had not improved at all I saw him playing table tennis and I told him that I wondered if was not better as he was able to hold the racket that had been touched by other players. He said no, he was still washing. A few days later, I saw him after playing and he did not go immediately to wash his hands. Again, he insisted that the obsession remained the same but as the following game between two patients was so interesting, he decided to postpone his washing. A day later he admitted he had gained a lot of control over his obsessions.

That's how we started with clomipramine, then we did a double blind comparing intravenous with oral but the person who had the codes suddenly died and we were never able to find the codes for these patients, which was a big disappointment. But what we described in this period still holds today, even though they were open studies which today isn't considered sufficient for any development of new ideas but the proof of the pudding is in the eating. Just recently I have finished a double blind study comparing clomipramine with one of the new anti-serotonergic antidepressants and clomipramine seems to work a little bit better.

When you began to see this happening first, how did you explain it? At the time it was thought that most of those who had OCD were also depressed and many people would have thought an antidepressant was working on that component of the picture.
No. To us it was very clear that neurotic disorders were related to depression but they were different disorders. It was not that OCD was a form of depression or something like that. At this period of time my main work was not in this area in fact, it was in the

area of masked depression and I published a book on masked depression but there was nothing about OCD in this book. It was very clear that the anxiety disorders, obsessive disorders, phobic disorders and so on were different from depression, were different nosological entities and the treatment was different. Also we didn't have an explanation why clomipramine worked so well and why the other antidepressants didn't. It was Yayuria-Tobias, an Argentinian, who said that it was probably the serotonergic aspect of its action that was important. At this time I was also working with serotonin - we had done a replication of some of the early Coppen work adding tryptophan and later 5-hydroxytryptophan to an MAO inhibitor and this worked very well but the idea of serotonin involvement in OCD was Yayuria-Tobias'.

At the time when you were using Clomipramine for OCD, the impression I get is that Geigy weren't awfully interested in the drug, it was..
I think they were interested in the drug but they were even more interested in masked depression. Actually the concept of masked depression, in some countries like Germany became, in the end, not so interesting because the promotion of drugs to be used across fields went almost too wide, so that everything which could be treated with antidepressants became masked depression. This expanded the market but with little credibility in the end.

Where did you get your ideas on masked depression from in the first place?
Well when I did my PhD, my father gave me the suggestion to do research in this field. Actually he had described in his work with neurotic disorders, not only the psychological symptoms but also the somatic manifestations of anxiety, and he thought that there were also many somatic manifestations of depression and that these could be or should be well described because patients would not look for the psychiatrist as a first option in these cases - they would go to other physicians. That's how this whole field started for me. I started selecting patients from different parts and looking at them, their symptoms, how the symptoms changed, which ones remained, how they were combined with each other and so on. What were the tools for diagnosis. Geigy were interested in this because of their interest in the field of antidepressants. They had promoted a group, called the Committee for Diagnosis, Prevention and Treatment of Depression. This was a group set up by Kielholz and supported by Ciba-Geigy for many years. Now this group is supported by Eli Lilly. It's the group which started the teaching of depression for general practitioners.

An early Defeat Depression campaign.
Yes it was around 71/72. Now the World Psychiatric Association has joined efforts with them to develop a new educational programme in this area. It was supported by Ciba-Geigy for many years and some people in the company were extremely interested in this area of knowledge. They were less interested in OCD in the sense that OCD was considered to be a very rare disease. But I think they were interested in this drug for a period of time.

Have we gone too far in the recognition of depression in the sense that in the 1960s when people looked out at the range of nervous disorders there were in the community it wasn't obvious that these were all people who were depressed. A lot of them were thought of as being anxious but now everybody's seen as depressed and you rarely hear of a primary diagnosis of an anxiety disorder.

Well there several things involved with this. One is there is an over-lapping of symptoms between the anxiety and depressive disorders. Second patients with anxiety tend to develop in their evolution, depressive symptoms. I think these symptoms should be considered more often than not a secondary depression. This happens in OCD, it is very clear but it also happens in panic disorders. We have done a follow up of anxiety disorder for many years. I have seen that they in the end have developed depressive symptoms, and somatising symptoms also. For a physician to use a drug which is called an antidepressant, although they could be called something else because they are not only antidepressants - they do other things, it's easier to justify if there is an underlying diagnosis of depressive disorders.

Indeed but how do you rationalise the fact that these drugs work on more than one illness. What are they really working on. Clomipramine clearly works on mood disorders. It also works on people with OCD and..
Well, the drug works on serotonin, which is clearly a very important neurotransmitter to modulate mood and behaviour. Second, most of these drugs, especially the tricyclics are not clean drugs, they have multiple effects. Usually this is seen as not very desirable because of side effects but sometimes it may be good because the influence on a number of different symptoms may help the individual to reach a better balance of function. In the past, the fact that there was a very striking modification of a severe disorder, major depression with melancholia, with a drug was a very impressive clinical development and this took precedent accordingly.

Okay. Working on 5HT is one thing but is there some common psychological element that these drugs work on, some antecedent for both affective and neurotic disorders. Would it in any way make sense to say that Esquirol in 1838 made a mistake when he split off the affective disorders as something separate - that they are actually downstream from something else?
I don't like the expression affective disorders because affect is something more restrictive than mood. Mood can mean many things. The concept of mood in German for instance, Gemüt, sometimes refers to the whole of psychological life. Kant, the philosopher, uses it this way. He said that "Geisteskrankheiten sind Gemütskrankheiten", which means that mental disorders were mood disorders in this sense. That's why I like the expression mood disorders as in ICD 10 and DSM IV, with the affective in brackets - I don't think the word affective describes all mood disorders.

Another thing is that when you look into schizophrenia or other disorders, you always find some kind of abnormal mood in many of the symptoms or manifestations of these disorders. But even so these are different disorders, from an evolutionary or genetic point of view or from point of view of their manifestations. The schizophrenic disorders, depressive disorders and anxiety disorders are distinct but always there may be some over-lapping of symptoms. There may be some common mechanisms for these symptoms and in some cases it may be difficult to make a diagnosis of depression for instance but I think it is better to keep them as separate disorders. I am not very much in favour of the single psychosis, as Janzarik and others, such as Llopis in Spain and others have suggested.

There is a middle European concept which you don't find in the UK or in the US, which I have found it hard to get anyone to explain to me in a way I can

understand - this is the concept of vegetative dystonia. What kind of relationship, if any, did that have to masked depression?
This has more to do with masked anxiety. In the work of my father with anxiety and neurotic disorders, this was one of the core issues. My father had spent some time with Hess in Switzerland and studied the hypothalamus and had correspondence with him on the areas which later McLean called the triune brain. It is also related to the studies of stress by Selye, the whole system which maintains our internal stability, our homeostasis. Sometimes the system does not work properly or over-reacts. Disorders of stress can kill the person because the reaction against stress becomes more important than external aggression and the individual may be killed not by the external agent but by their internal reactions. The corticoids are “cell tranquillizers”. The other side of the coin is anxiety and anxiolytics. Bakan a psychologist in Chicago, who migrated to Israel, wrote a book on the parallelism between Freud's and Selye’s thinking, between psychological and physical homeostasis and the self-destructive mechanism in psychological homeostasis which Federn called thanatos. It is so destructive that it is called the death instinct. All this is related to the vegetative side of the anxiety disorders. Vegetative dystonia may be the expression of a masked depressioin but also of an abnormal stress reaction.

Is it a somatisation issue then.
Yes. It's the somatic correlates of anxiety. Every affective state has somatic correlates - tachycardia, sweats, movement, whatever you want. The philosopher Sartre interpreted the role of emotions as a need of the individual to survive in a world where rational interpretation is not possible anymore and the vegetative correlates of every emotion are the serious part of them. This implies that when an individual has to face the loss of a loved one for instance or an overwhelming threat mechanisms appear to allow him/her to survive both at the psychophysiological and psychological levels. In the first case, the withdrawal from a world which has no meaning without the loved one, in the other a preparation for fight or flight. It is always like that and the whole theory of psycho-somatic medicine was born around this concept. My father studied this closely because as a clinician the somatic aspects of anxiety were very important to him. In this school of thought it is not only aspects of the psychodynamic state that can cause a problem. Psychosomatic medicine held that there were some states, some vicious circles which created and maintained the symptoms of what is called anxiety or stress in Anglo-Saxon words or nervous diseases in the old English tradition or neurasthenia or other concepts such as vegetative dystonia in the German speaking world.

At one point Geigy marketed Opripramol for this - Insidon. Did it actually work for these conditions - neither the drug or the conditions ever got to the UK or the US
It was very good and very widely used for people with minor anxiety symptoms. I can tell you an anecdote. Once a healer came to me who wanted his wife treated. She had a mild depression and I told him “You know very well how to deal with this - I am sure you see lots of these people”. He said “yes and I also know which things work and which things don't work but with things that I usually have success these have not worked with my wife, that's why I come here”. So I asked him what he did with his people and he said “well I tell them what they have or I tell them what they have to do to get better and then I give them Insidon”.

This popular healer had very quickly learnt that this drug worked for states of anxiety and mixed anxiety and depression with a lot of somatic manifestations. It is very interesting that when you look at DSM and ICD 10, in anxiety there is always the mention of the importance of somatic symptoms but this is much less the case in depression.

This is where your work is interesting because you have always emphasised the somatic and vegative symptoms of the mood disorders as well but I'm still finding it hard in my own mind to tease these apart from the vegetative components of anxiety.
Well there is an overlapping of anxiety and depression. But essentially they are different because most of the symptoms of anxiety show a hyper-reactivity to external stimuli, the body is hyper-responsive, while in depression the main characteristic probably is inhibition - dry skin, dry hair, constipation, pain - everything which has to do with inhibition.

Is Insidon an antidepressant or an anxiolytic?
I don't know. It was marketed very quickly with very few studies. The idea was a very funny one because Insidon has the structure both of an antidepressant like Imipramine and an antipsychotic like Chlorpromazine. It wanted to be a drug which worked for depression and for schizophrenia at the same time but it did not work for severe depression or for schizophrenia. It was marketed and it worked for these mild anxiety symptoms.

Is there a certain sense that during the 1960s you had a range of compounds, such as amitriptyline, clomipramine and Insidon, all of which were similar in some respects, but which have turned out to be rather different clinically and perhaps we are just beginning to appreciate more today how different they are to each other. But in the 60s, the companies in order to get a market had to decide on the compounds fitting into one or two groups. They were either anti-psychotics or anti-depressants. There was no room for anything else.
No, we had room for something in between. We had Insidon, we had Melitracen, which was a drug which was marketed in Germany. You had some groups of drugs which were used for mild psychiatric conditions but all of these disappeared when the benzodiazepines came to the market. There were others like meprobamate which were used for minor psychiatric disorders and which were also called minor tranquillizers. All these vanished when Librium and Valium came on the market but these conditions and agents existed and should not be forgotten about.

Let me move into another area where there is overlap and confusion. In your ECNP plenary lecture yesterday you addressed the topic of the personality disorders. When did you begin to move into that area?
Personality disorders may be linked to the anxiety disorders and masked depression as there are behavioural masked depressions, which are quite common in childhood and adolesence. The mood disturbance is expressed, not as a complaint of mood disturbance or as vegetative symptoms but as behaviour, which is unexplained. Second, when you treat patients with psychiatric disorders, where you have also some kind of personality disturbance and this changes also during the treatment, you have to postulate that they have something in common. A third point is that dualism remains

very much present in psychopathology. Kurt Schneider, for instance, in his description of personality disorders and neurotic disorders was dualistic and this has created many difficulties in this area.

My father and I published in 1974 a book on the Experience of the Body, which has some philosophical aspects to it - it was influenced by the German anthropological approach. It covered body image, body experience and so on. One of the chapters was about the limits of dualism. From this point of view it followed that it was necessary to look into the biological substrate of personality, the way we are shaped. We are not shaped in two parts but in one part. From this came my scientific interest in this field. We then went on to some studies with CSF in depressed patients, using serotonergic probes - such as fenfluramine. We were interested in suicide and we did some studies trying to look at suicides in subjects who were not depressed. These people did not fit the criteria for depression - that was an exclusion criterion - but they all could get a diagnosis of personality disorder. In a sense it was a waste basket diagnosis when you take away psychosis and depression but these people are something - most of them were borderline, some were hysterical and the findings were interesting.

Then gambling started in Spain. After the death of Franco, casinos slowly opened and people started gambling and of course, some after a few years became gambling addicts, pathological gamblers. I have been interested for many years in this because a behaviour like gambling is like an addiction without the drug. It seemed a good model to study this kind of behaviour, without the influence of the drugs. Dr Saiz in my unit and I became very interested in this group and we set up a programme for pathological gamblers with psychological and biological treatments. One day we decided to compare these with more “normal behaviours” in bull fighters and explosive experts, who also take risks but in their professions. This study was done with Drs Carrasco and Saiz who had done his PhD many years before correlating personality variables and biological findings in normal subjects. So the idea of studying the biological aspects of non-major psychiatric patients had been present in our group for some time.

Explosive experts did extremely well on the psychological tests. They proved to be highly controlled, low in sensation or novelty seeking and very rational people. This was natural if we remember that these individuals have been selected through a strict procedure and intensively trained. Bullfighters on the contrary were high in sensation and novelty-seeking and extroversion. The controls were in the middle but the gamblers performed even higher than the bullfighters on sensation and novelty-seeking.

The results from platelet MAO activity were very interesting as pathological gamblers had the lowest activity and as a group the smallest variance. The rest had higher levels of activity distributed under a wide bell shaped curve. In the three non-patient groups there was a correlation between MAO activity and novelty and sensation seeking. We interpreted this as a consequence of two phenomena - a dimensional model that could be applied to non-patients with a correlation between biological and psychological measurements and categorical differences between healthy subjects and pathological gamblers.

Some time later I became a member of the Royal Academy of Medicine in Spain, a very important and honourable institution in our country. When you are elected, you have to make a speech, usually of a historical value and devoted to a consideration of a specific topic. I thought that the most challenging would be to describe this area, so I devoted some time to put in order my ideas and to fit the pieces of our research together. That's how the interest developed. It has really been a fascinating group of people because they have been very neglected. They are very difficult to study because they are very difficult patients to relate to, they create a lot of problems in the doctor patient relationship, they are difficult to follow in the lab and so on, but in the end they are a group who suffer a lot because of this disorder of personality.

When you began to move into that area were you aware of any one else working in the area?
Yes, of course. I was very much aware of Eysenck's work. I had been at The Maudsley, so I met him in some of his sessions and lectures. I still remember one day when he came in and said that now for the first time we have data which show that behaviour therapy is better than phenelzine. He was elated by this. But he had an interest in correlating traits with biological variables and he had a very good statistical approach to this work and I was very much aware of this. More recently I was aware of the work of Zuckerman, who helped to open up this field and then of course the work of Cloninger, Siever and Davies. I was also aware of the studies of suicide and impulsivity by Cocarro, Marie Åsberg and others. I was also very struck by the study of Brown in the States, who showed in a population of non-patients, men in the Army, that there was a correlation between violence, impulsivity and low 5-HIAA, the metabolite of 5-HT in the CSF. It was the first time that such a strong correlation was found in people who could not be considered as patients.

In one sense you are saying, it would appear to me, that one of the conclusions you can draw from all this is that biological research on the psychoses is doomed if we are not controlling for personality.
In a sense yes. You could say that genetic research, for instance, is more related to personality - i.e. in the vulnerability hypothesis of schizophrenia. In the Danish study on schizophrenia, the genetic element is manifested in schizotypal personality disorder, which may or may not become a schizophrenia, depending on some other external circumstances. So perhaps in this sense, the genetics of the personality is more important than the genetics of the disorder.

In one sense that has to be true when you think about it but we don't think about it that way now which raises a range of other questions. When I suggested to you earlier that someone like van Praag was seen as being in league with Satan when he was looking at the biology of the major disorders, there is almost a deeper problem it seems with the biology of personality and temperament where people have felt there are Nazi connections or something like that. Irv Gottesman or Markku Linnoila working on this in the US have to be very very careful what they say to which groups when because it is seen as having a right wing agenda of some sort. You must be even more aware of this than I am.
The States is a very strange country in this context. When you look at the discussions between the creationists and the evolutionists - it's actually a ridiculous discussion from

every point of view, scientific and religious. They tend to take the part for the whole of things. They have a very narrow scope sometimes . The fact of being biological does not mean that something is inherited genetically. The best research on this question or hints about what can happen are the studies of Sapolsky, which I learned about because of our studies on this group of violent suicidal people. We found in this group not only a blunted endocrine response after challenges but also a very strange pattern of cortisol secretion. Compared to controls at baseline, they have a high cortisol and when challenged this cortisol did not increase, while the controls had lower baseline concentrations which after a challenge increased significantly.

I looked everywhere to find an interpretation of this and similar findings. I found it, a little bit by chance, in one of the studies of Sapolsky, who studied endocrine variables and social status. As this is very difficult to do in human beings, he went to the Serengeti National Park in Kenya to study the baboons. There he found that baboons high in the hierarchy, in normal conditions, had low baseline cortisol concentrations in blood and high testosterone concentrations. Those lower in the hierarchy had the opposite - high cortisol with low testosterone. Under stress those high in cortisol increased slightly or not at all whereas those who were low went high. These latter had a good adaptation to stress but those with high cortisol were clearly chronically stressed and they could not react to another external stress - they were working at the ceiling of their possibilities.

You might think that some baboons are born maladapted and that's why they go higher but that's not true because sometimes baboons organise revolutions just as human beings do and in the revolution everybody has high cortisol and low testosterone. I often say that the hippies were right when they said make love and not war because you cannot have high cortisol and high testosterone at the same time. After the revolution the same patterns reappear but this pattern was independent from the pattern that the same baboon had before. So social rank has an impact on the pattern of secretion of cortisol and testosterone. Sapolsky developed this looking into CRF and other mechanisms and established that this is a brain mechanism. So there is a biological background to how individuals respond to stressful situations but according to social rank.

Now in our studies, the controls were mostly medical students and young physicians, who are very privileged people in society which protects them, teaches them, puts them in big hospitals with the best teachers. They are very high in terms of social privileges, compared with the people who are unable to face frustration, which means unable to cope with some external stressor - these were the ones who were admitted to hospital because of impulsive suicide attempts. So although we have biological findings, the origin may be social. It's not fate that you are born like that and you will be like that necessarily.

But in order to understand these issues, you think we must understand the biology.
Yes of course.

Why has the study of temperament been so underplayed in the last 40 years. Is it because of the Nazi programme or is it because the drugs when they came out,

in contrast to what Eysenck's theories would have predicted which is that we would find drugs which would alter personality, in actual fact the drugs were agents to treat specific diseases or at least they were sold that way. Is it because it has seemed easier to go down the disease route that we have neglected the biology of temperament so much. In the mid 1950s, it was very respectable to look at constitutions, at body build and things like that, but all of that's gone out of the window, at least at the moment. What's the reason for this eclipse?
Well there are difficulties with this kind of research. It is very easy in a sense to work with somebody who is a patient now who was not a patient a few months ago and then when you give treatment and see a change and the person becomes what he or she was before the illness, you can take a measure and you can study a lot of things. But in the area of personality it is very difficult and this has to do very much with the notion of dimensions of personalities and traits. Traits are present everywhere. We all share the same traits with a little bit of variation but this is not stable. It may change with the time of the year, the time of the day or the environment. So work in this area is very difficult to do and that's why Sapolsky went to do it in baboons because it's much more simple.

It's also very difficult to put boundaries into these issues. One of the outcomes of our studies is the notion that dimensions are present in everyday life but you have a categorical difference when you jump into the pathological field. Coming back to the study of bull fighters and explosive experts, when I presented this at an APA meeting somebody said "now you have a treatment for these bloody bastard bull-fighters who cause such suffering to these poor bulls; are you going to give them fluoxetine?". I think the answer to this is that fluoxetine may help a pathological gambler or may help an impulsively suicidal patient but it will never make out of a bull fighter, an explosive expert. That's the difference.

What drugs do is to control some tendencies and what you see in diseases is that all these things which are a little bit more or less in us sometimes become autonomous, to use the expression of the English psychiatrist, Gillespie - he talked about the autonomy of these states as in autonomous depression. This means that we all react to the environment with sadness on occasions but sometimes this sadness becomes autonomous and then it's a vicious circle, which is difficult to get out of. When you treat personalities with drugs, what you see is that some of these traits which have become too autonomous, too conflicting are reduced and the person is able to find a new balance - a balance within himself or herself or in a relationship with other people. This is not the same as getting relief from a well-characterised symptom.

How do you read the fluoxetine phenomenon. Because this, in one sense, could be seen as the return of the repressed idea that maybe drugs could act on the personality rather than on a disease.
Yes Listening to Prozac was a very unfortunate book, in the sense that based on real descriptions of things that everybody has, Kramer expanded these points to a theory that personality can change, which means that human beings can change and the world can change because of a single drug - that we will be able to influence creativity and that people will never be the same again, which is nonsense. But the fact is that we can take away certain traits of personality when they are present in an extensive

and dominant way in people. Now this can be considered as a disorder of the personality but treatment will not change the whole personality of an individual.

In your lecture yesterday you mentioned that in recent years there has been a migration of certain personality disorders from being seen as Axis II disorders to Axis I disorders. When did this begin to happen and has it been happening because the drugs have begun clearly to have an effect on what have seemed to be personality disorders - like the RIMA's for avoidant personality disorder - giving people the feeling that personality disorders perhaps are treatable entities.

There is another issue we should touch on first which is the distinction between personality disorders and variants of personality. This is often confused and it is confused in DSM IV and this I think is an error from the conceptual point of view. There are difficulties present but this does not mean that we should not try to identify a group of people who have disorders of the personality, which are not just a little bit different from the norm, as we all are from each other. This confusion is what leads to the kind of generalisation in Kramer's book. When you don't make this distinction and you find that some personality disorders have a biological pattern or respond to some kind of treatment, what happens - people say well these were not personality disorders after all. They are something else. So that is why certain personality disorders have been moved over to the illness axis.

My approach to this would be to keep these disorders in the personality disorders group, and say that they have a biological pattern which can be treated just as the major psychiatric disorders can. I have nothing against having schizotypal personality disorder either as a personality disorder in DSM IV or as schizotypal disorders within the spectrum of schizophrenia as it is in ICD 10. I don't mind having epileptic personality or organic personality disorders within the chapter of personality disorders. You could have cyclothymic personality, or dysthymic personality instead of dysthymia or cyclothymia provided you explain what these are and how they can be treated, how they can be diagnosed and so on. There is also avoidant personality which is becoming one of the anxiety disorders. But I think this migration is bad. In the end there will appear to be no personality disorders but I think we will come back to Kurt Schneider's expression "personality disorders are dead, long live personality disorders".

Did he actually say that?

He says that every generation tries to kill the concept of personality disorders.

You find within psychiatry that people react viscerally against the term personality disorder. Many people feel you are doing patients a great disservice to label them as personality disordered.

In DSM you are forced to label people when you give them an Axis II diagnosis. You don't have this in ICD 10 in this sense because in the multi-axial version you have Axis III, where you have environmental conditions and life-style, you can always tell the person his or her life-style makes them vulnerable for certain disorders or problems. This is not a diagnosis. Type A behaviour for instance, this is not an illness or a personality disorder, it is a life-style. You can discuss why some people have this life-style and others have another but this is not a clinical diagnosis. But where do you put

type A behaviour in DSM ? - either you cannot put it anywhere or you put is as a personality disorder, which it is not and this is really not a very good approach.

As I've said the whole area of personality is one that people haven't wanted to talk about for 10 - 20 years, but is the vulnerability hypothesis in one sense the politically correct language for referring to this area?
Well yes. You have personality disorders and variants of personalities and of those some are relevant for medicine, some are irrelevant. Those which are relevant for medicine are relevant because they imply a certain vulnerability or they are often associated with disorders and you will have to manage these aspects of the case when you are dealing with risk factors or dealing with the rehabilitation of patients and that's why some are relevant and others are not. But it depends on what you are doing. If you have to lead a team, all kinds of personalities come in - they are relevant for your work but they are not personality disorders. I think we have to make the distinction very clearly between these personality traits which may look abnormal and pathological but not to the degree of the higher psychiatric disorders. They are limited to this aspect of a situation, they are different from other personalities, they may be very awkward or very different but nevertheless they are not pathological.

Now, despite working in an area that is politically tricky and despite coming from Spain, you have been very influential on the world psychiatric stage. You are involved in the WPA, you were involved in ICD 10, which along with DSM is one the major political blocs in psychiatry.
I have been one of many persons in a very large taskforce. Secondly ICD 10 is very much influenced by DSM III, which is is quite natural. The change from DSM II to DSM III was the important change, a change of historical proportion. DSM IIIR, IV and ICD 10 are improvements but the real change was from DSM II to III. Nevertheless, there are some differences which are important, which came about because the taskforce for ICD 10 was much more international. Many different schools of thoughts had to be accepted - the clinical psychopathological tradition of Europe is more present in ICD 10 than in DSM but if you look at the taskforce of ICD 10, the largest number are people who were involved came from the United States. This was very natural and it should not be seen as opposing blocks. In ordinary clinical conditions, it is irrelevant whether you use one or the other. The differences are minimal and really only present in situations where we have no data to make a decision. There are some other cases such as neurasthenia, which is not in DSM because nobody uses the term neurasthesia in the States but it is in ICD 10 because in some parts of the world it is used.

There are two main differences; one has to do with this personality issue which is tricky and difficult. It is difficult to produce research to convince people and it is difficult to say that one perspective has more advantages than the other. This remains open for dicussion. Another one has to do with the degree of disability, which is important for making a diagnosis in DSM but not in ICD10. This is because disability is related to the environment and this may change from one country to the other, so it is more difficult to establish a criterion for disability. In the States if you don't have either suffering or disablement, the symptoms count for nothing because they don't want to be accused of making a disease of a social condition. For instance when does shyness become social phobia? - is it when it produces a lot of suffering to the person, or when it

produces a significant disability for the performance of a job. This question of disability as a criterion for diagnosis is not taken up in ICD 10 but both points of view have good reasons to exist. We are are in a transitional period for some years and we will need to find a good solution to solve this.

Can I ask you about Gerald Klerman. He was one of the key driving forces behind DSM III. What did you make of the man and his approach. He was very Kraepelinian in one sense.
Klerman was a very intelligent psychiatrist, very knowledgeable, very interested in everything and with very large views. I see him as one of the most European Americans in this context, no doubt. But the idea that all research had to be done based on symptoms etc I would describe more as the Robert Spitzer style than the Klerman style.

You were involved as well in the Alprazolam studies for panic disorder, which were set up by Klerman, what did you make of all that, because the disability issue comes in there as well.
Sure. I was involved in that. It was a period that was very bad in Spain, there was very little money for research. Things had changed with the death of Franco and nobody knew where research was going, we were in a bit of disarray, so it was opportunity to do a large study with a very large international group with opportunities to travel to meet people and this study was therefore a very important experience for many of us in Spain. The study was disappointing however for a number of reasons because it did not show any important advantage for alprazolam over imipramine and the follow up was not encouraging. The placebo response was also very big in this study, which of course is something you would expect in this kind of patient given that there was a lot of interaction with doctors. When a patient went through this study, he had gone through more hours with the doctor than in most kinds of psychotherapy. It was more than 5 hours per week. Of course I would say nothing negative about the skills of a psychotherapist but there is the question of personal contact as much as the question of the actual skills to do all this. I mean the patients will need to be reassured and so on. It was very funny to see that this placebo response was different from one unit to the other and from one country to the other, which showed very clearly how patients were recruited and treated in each country, or how humane was the group treating the patient or how rigid and less humane.

On the question of disability, panic disorder is a very disabling condition and Klerman's studies proved the degree of disability and the suicidal risk. This appeared in the study and it appeared in all the countries involved. Societies are human constructs, what people believe about themself and the world and the nature of the world plays a role but certainly this disorder was very similar across the world regardless of the setting.

That's kind of surprising, I guess.
Not if you really think this is a disease. Yes if you think that it is a human condition, in which the social side plays the primary role.

What did you make of the controversies that grew up between Klerman and Isaac Marks and the correspondence in the British Journal of Psychiatry. There isn't anything else quite like it in the psychiatric literature.

I was sitting with Marks when Klerman presented the studies at the APA meeting and we were discussing these things. Marks, I think , was in a period of positive disappointment. All his studies of behaviour therapy with OCD were in a period where the serotonin bandwagon was begining to roll, so his research and the other things they had in OCD were not so attractive for many people in this period. So, he was trying to protect his position in the field. He is a real fighter and a very knowledgeable person and I think he was able to pull out of himself the best of himself to make a critique of these studies, although I think he went a little bit too far. The results of the study were clear and evident - they were not as promising as Upjohn had hoped, although they were solid and important and relevant. People are now using alprazolam to treat panic all over the place. One has to think of the setting and whether the patients are suited. Every general practitioner in the country, can treat panic disorder with alprazolam or maybe with some of the antidepressants but in most parts of the world, even in the United Kingdom there are not many units, like Mark's Unit, to do behaviour therapy.

Secondly we are in period of time, where we are starting to realise that behaviour therapy as such does not exist. Biological psychiatry as such does not exist either. It is specific drugs for specific diseases. Specific techniques for specific problems of specific disorders and this kind of specificity leads to the notion that what works in OCD does not work in phobias and what works in phobias does not work in depression. The development of techniques which will be better applied for different disorders and should be available in the training of physicians is coming but we are not yet at this stage. So there was the scientific discussion of panic on the one hand and the other aspect was what is relevant to medical practice in many parts of the world.

Coming back to the international perspective, the ICD 10 meetings have to have been rather extraordinary in that you had the input from all different traditions in the world. The Chinese for instance have more neurasthetics than all the patients we have got in Europe put together probably.
Very much so and then I was also was present in meetings to discuss DSM IV and ICD 10 - to find some consensus. That was also very interesting because you learn very quickly where the limits of our knowledge are and where we need more knowledge. ICD 10 and DSM are different because we don't, for instance, have the knowledge to decide whether 2 years or 2 months worth of symptoms are needed to make a diagnosis or whether we need three symptoms out of ten or five out of fifteen or whichever. All these differences are there because the problem has not been subjected to enough research but it will be clarified in the future, I hope.

Can you fill me in on your involvement in the World Psychiatric Association and what you perceive its role to be in World Psychiatry.
Well the World Psychiatric Association began in 1950 as the society to organise World Congresses in Psychiatry. The first one was in Paris and it was a Congress of Reconciliation between German and French psychiatry after the War. Then it grew up in a very important way during the period of Cold War confrontation with the dissidents issue. This consumed a lot of energies and money from the WPA. Once it was solved the WPA was ready to play a role in education and in facing new challenges.

One challenge has to do with the common diagnostic language all over the world. Another has to do with trying to promote the exchange of information around the world.

Another has to do with increasing the ethical standards of the profession. A concern with the ethical issues began in the 1970s with the Hawaii declaration which was born in the period of the political abuse of psychiatry. Now this has almost disappeared and all over the world the foremost issue is the discrimination and stigmatisation of patients which is addressed in the Madrid Declaration. This is a more refined declaration. Discrimination against psychiatric patients is present all over the world and the Declaration raises the status of the patient with psychiatric disorders to an equal partner of the psychiatrist, which is a very important concept and very well formulated.

This was put out at the recent (1996) World Psychiatric Congress in Madrid?
Yes, that's why it's called Madrid Declaration. The WPA has an Ethics Committee who looks at these issues, who is concerned with challenges for the profession. Each time Ethics Committee members are appointed, they change every 6 years, they start afresh and look at what are the issues and that's how this Ethics Committee produced this Declaration.

There were issues which were not present in the Hawaii Declaration, such as organ transplant, sex change and addressing these led them to consider how they might find a more general formulation. The original resolution was born from a group who had very much the notion of political abuse in psychiatry but this could change and when new people came in the ethics committee changed very much. In the first version psychiatry was seen as an agent of social control but in the second the status of mental patients was considered in a more positive way. So it was with all this in mind and all this background, that the Madrid Declaration was born.

One of the critiques you could raise about groups like the WPA is the potential for diagnostic imperialism. The people who can put the resources into an education campaign, at present, are the drug companies who are wedded to a Kraepelinian model which is working very well for them and their compounds at the moment. Are you going to educate the world to suit the industry?
Well the WPA is better prepared than many other international institutions and the reason is that we are an association of member societies, which may be less easy to influence than a single large organisation. But in the case of many of these member societies, their interests go beyond what has to do with drug treatments for psychiatric disorders. They have other interests and they have other views. Then you have a lot of sections in the WPA and most of them deal in topics which are not relevant to biological psychiatry, nor for psychopharmacology - the place of women in psychiatry, forensic psychiatry, social psychiatry, victims of abuse , epidemiology and many other things. So we are less prone to the kind of influence you mentioned - the idea that there are specific disorders, which should be treated by a specific drug, which happens to be produced by a specific drug company.

The WPA had produced guidelines to address specific issues for which we need sponsorship, which companies could help sponsor. But, for instance, at the World Congress we had CME credits for the American participants and we had to produce conflict of interest declarations regarding sponsorship following the standards of the American Medical Association. The application of these standards may not be perfect but still there are some standards that address this issue. In the Congress in Madrid we tried to identify very clearly which were the industry sponsored symposia, which

were industry supported and we are going along this path as much as we can. We have to be independent from all these pressures and I think we are better than many other associations. For instance, if you look at the composition of the WPA Executive Committee you will find more often than not people who have not been involved in drug research or in psychopharmacology and the same happens with the leadership of most of our member societies - The Royal College of the UK, the APA in the States, or the Royal Australian College of Psychiatrists ...

In the case of this ECNP meeting here, there seems to be a disease model oriented form of psychiatry, very Kraepelinian in one sense, more than in any other society I can think of really; there's a greater focus on the disease entity and the drug treatment of the disease and much less on, for instance, the basic sciences input.

Well the ECNP is a neuropsychopharmacology association like the CINP or ACNP. There is perhaps less focus on diseases in ACNP because if you compare the huge amount of basic research done in the States with the amount done in Europe then you can understand why the impact of basic research is very important in ACNP much more so than in ECNP. The drug company presence could be as large here but drug companies in the States are doing more research compared to the research in the central nervous system in the European companies and so you can understand why many people who work in the laboratories of drugs companies in the States go to ACNP but for many laboratories working in the central nervous system in Europe they are probably all here but you cannot see them.

Second those are associations which are in the field of neuropsychopharmacology which is about the rational application of and the development of drugs for treatment of disorders and I think that the concept of specificity is very important to do with disorders. If you don't have a diagnosis, you have the Kramer approach. We need a diagnosis. We are not like psychoanalysts or psychiatrists who don't need a diagnosis, who think that a diagnosis may harm the patient and who just apply psychoanalysis to everybody who is willing to come and pay money. That's not the approach of medicine. The approach of medicine always is related to specificity, to the notion of morbid species. So I don't see a real problem in this. I see a discussion on how psychotropic drugs should be applied to the treatment of schizophrenia or depression or panic disorder because essential in clinical trials to compare drugs and to ask whether drug A is a better drug than drug B. In order to get an answer you have to ask for what condition or for what symptoms of what condition are we talking about. So I don’t see that specificity by itself is bad. It may be abused but that's a risk.

One of the things that hits me about that is that there have been clearly a lot of people from the Spanish-speaking world who have been working fairly intensively in psychopharmacology but the credits for some of these developments don't go to people who have published in Spanish. You mentioned Yayuria-Tobias earlier.

Well one reason for this was the conditions to do the work which were much more difficult. In my academic career I had to move several times, I am now on my 4th place, and in the first three I had to start my department from zero - no staff, no facilities, nothing. So it took a lot of time to create something and then once it was created I moved. There was that lack of stability. This has changed. Our country is

very different from what it was 30 years ago but this created problems for anyone who wanted to do research of sufficient quality to be accepted. Then many things were published in Spanish and while we think the Spanish language is a very important one, not everybody thinks the same thing or reads Spanish.

In one respect it may be the most important language in that probably there are more people actually practicing psychopharmacology in Spanish, but it has been the Anglo-Saxon and German influence that seems to control the organs of publication and things like that. This is relevant here in that when you go into the history of biological psychiatry for many of the developments, such as sleep treatments, ECT, psychosurgery, the earliest use of the phenothiazine nucleus by giving methylene blue in affective disorders, you can usually find Spaniard or Italian who has done the first work in the area but they are usually don't get the credit. In addition, among the founder members of the CINP there were quite a few people who were from the Spanish speaking world. Who for you have been the key thinkers?

In psychopharmacology, biological psychiatry or in psychiatry in general, I would prefer to speak of groups. For instance first in South America, you have in Chile a group of very good thinkers, in psychiatry and in psychopathology. In Chile they have very good medical schools and the training of physicians is excellent and they are good in other specialities as well. In Buenos Aires, which is the city where you find the greatest variety of psychiatrists, you have also an important group of people. It is not Spanish speaking but in Sao Paulo there is a group of people oriented in biological psychiatry also. So there are several groups. There is not one person now. We are not any more in the period of single personalities, it is a matter of groups and I would say that these 4 cities have groups of people, who do a lot of work and who are becoming and need to become more and more important.

You have to remember that South America has gone through an extremely difficult economic situation. Political and economic. In some countries for some years you could not import books. So this has produced certain drawbacks in say books, equipment for research or opportunities to travel for instance. This is changing very quickly I think but it will take a few years and I think the situation will change very much in future. And of course in the case of Spain, we are now part of Europe.

There's one way in which Spain hasn't been part of Northern Europe - the regulation of the pharmaceutical industry in Spain has been different to that in the US and UK; it's been somewhat easier and more flexible. Drugs have been available over the counter that haven't been available in North Europe. Now you find these witchhunts happening with the benzodiazepines in Northern Europe but do you have them in Spain?

No on the contrary. With regard to the consumption of benzodiazepines this was relatively low compared to the UK or France up to 10 years ago, even though the prescription and the availability was much more liberal. Now regulations tend to be more strict.

But, for instance, if you want to identify a problem I would say that the prescription by a non-psychiatrist of non benzodiazepines in Spain will become an issue of importance. The prescription of drugs which are supposed to be antidepressant and are not proven

to be antidepressants but which are marketed and prescribed by general practitioners is extremely high. We also still have drugs on the market which have never been proven to work or combinations of drugs some of which have ineffective or have very low doses in them and some are combined with a vitamin. These will disappear soon - not from one day to the other because it will mean closing some companies and putting more jobless people on the streets but I think this will change.

Is this always a good thing though. Because one of the things you hear in this part of the world is that the reason we haven't have had the breakthroughs in recent years compared with situation between 57 and 62 is that it is so hard to get the compounds on to the markets here in this part of the world and the thing that actually generates discovery is the range of compounds on the markets, people noticing something different the way you once did with clomipramine and OCD.
I think in Europe the drug industry was very much harmed by the anti-psychiatric movement. They moved away from the central nervous system. They wanted to work in other fields which are more acceptable to our social groups like cardiology or cancer or whatever you want. At the same time some American companies, following the spirit of the Decade of the Brain, concentrated in the central nervous system and that's why now they have a lead. European companies are beginning to come back. For the first time in a while I see a stand by Hoechst here which is very good. Lundbeck is here and although its a small company compared to others it's 100% devoted to CNS. Others are getting more interested. So, that's why the lead comes in a great part from the United States - they have kept doing research and the decade of the brain, also created a movement and that has helped their image.

It seems to me that impulsivity, for instance, is a very European concept really and while there is some work done by the US researchers on it, it's still the kind of concept that one associates with people like yourself and Herman van Praag rather than with the Americans. Is there some reason why concepts like that occur over here much more than over there....
I think in Europe we have a more tradition of psychopathology. In the States this never existed in the same way. The best example is again DSM, which is a-theoretical and non-psychopathological. Even the word psychopathology is not well understood in the States but psychopathology is the science that leads to an interest in anxiety, impulsivity and in other modes of behaviour or psychopathological conditions.

But there is an area here where the public, I guess, feels a bit unsure. When people are deluded clearly they're crazy but when someone's impulses are out of order there is the almost unresolvable question of whether they are bad or mad.
But I think here one should apply the principle which is essential, in forensic psychiatry, which is first you make the diagnosis and for this you have to study the psychopathology. First you need a diagnosis and then you study the responsibility of the patient. The clinical diagnosis is always the first step. If there is no diagnosis the boundaries are different. Its the same with the rest of medicine. You have to put some limits.

There has been a change clearly and we have moved people out of the mental hospitals and there's a perception that we are dealing with disease entities more

effectively than we were before. But if you begin to look closely at what actually happened when you ask some people is going on often the kind of message is clozapine, for instance, is a good treatment but it is not so much a great treatment for schizophrenia as a very good anti-aggressive agent and in some respects it could be argued that what psychiatrists do in practice comes down to the management of impulsivity and aggression and things like that. Now we couldn't let the public know that that's what we do. We have to say that we're treating treating disease entities.
Clozapine is a very good example to mention. Clozapine is not an anti-schizophrenic drug. There are no anti-schizophrenic drugs. Schizophrenia is a very complicated disease and clozapine is an anti-psychotic that relieves some of the symptoms. It works in hallucinations and with delusions and for some behavioural problems related to the psychotic symptoms. Clozapine may alleviate the impulsivity from psychotic symptoms which a schizophrenic patient might have but if you give clozapine to suicidal patients who has aggressivity against themselves or for the impulsivity or aggression that goes with sexual abuse cases it does not work. So first you need a diagnosis and then you treat the specific problem within this diagnosis. In the same way a serotonergic agent may work in some impulse control disorders, in bulimia for instance, but it will not work in the impulsivity of a schizophrenic which is different.

Okay, but there are ambiguities it seems to me in that to some extent you and I know they are not the treatment for Schizophrenia but the public has to be told they are a magic bullet for the entity that is Schizophrenia.
No. You have to tell the truth, that's why you have to speak the same language and the truth is that while you cannot treat schizophrenia without drugs the drugs are not the only treatment for Schizophrenia. Schizophrenia is a severe disease which needs treatment for many years and a lot of effort from the patient, from the doctor, from the family and so on. There is no easy answer just like there is no cure for cancer. You know that there are still things that you can do - but this is a common situation in medicine.

I think that psychiatry now is at a very important turning point. At the World Congress , I had at the end to do an interview on television and they asked me to make a summary of the Congress. I said well I can make it around the theme of one world, one language and what this means. It means first that we psychiatrists should speak the same diagnostic language among ourselves, we should have the same protocols for interventions, the same outcome measures and so on. We are a single community dealing with the same problems. Secondly we have to speak the same language as the rest of medicine, which means we have to learn the language of primary medicine and we have to teach our language to the rest and this is very important. Third we have to learn to speak the same language as science. We are part of neuroscience and I always like to say this in the singular. Fourth, we have to speak the same language as our patients and I think the Madrid Declaration is a good example of what can be done. And fifth, we have to speak the same language as society in general - we have to open our doors as much as we can and we have to have an impact in the press. We had a big impact in Madrid and I was impressed by two editorials 6 days apart in one of the big Spanish journals. The first day of the Congress the title was "Psychiatry from mental hospitals to Science". It described the perception of society and the changes we have actually achieved. On the last day the same journal had

another editorial on the Congress entitled Psychiatry opens its Doors. I think that this is a really big change in our profession.

When you made the point about psychiatry and neuroscience sharing a common language, do you see psychiatrists evolving into clinical neuroscientists?
No. I put the example of research in neuroscience in the statement but neuroscience is also changing. When you study the molecular genetics of behaviour or the field of social biology, neuroscience is not only concerned with what is happening within the central nervous system but with an individual in their environment and within this larger scope the interests of different disciplines come together to the study of brain and behaviour in disease and under normal conditions. But in this sense I was thinking more as a clinician, that we have to open the door to the lab and to those who want to do field research and sociological research.

As a symbol though would it help if we were to become clinical neuroscientists rather than psychiatrists. Psychiatrists are always going to be soul doctors in some sense and what you're saying really is we need to be more effectively treating medical problems rather than disorders of the soul.
I think that we should defend our medical identity and that we are dealing with an important part of medicine - we are not magicians. What is the soul? I don't know but I know where I have to find how the soul works, the mind is the brain in action. I think we should define ourself as physicians first because there is so much to give our patients and that's our basic mission - to treat patients. To treat patients and to try to help them to get some of what they are missing in this world. I see myself as a physician first even though I do many other things - I teach, I do research, I am member of the Board of a Health Insurance Company - but the bottom line is that I am a physician. All these other things I think interest me because of issues, which play a role in our profession. We are not politicians. We are not sociologists. We should not lose our identity as clinicians. That's why I like the WPA very much because it is an association of clinicians. You have everything there but the bottom line is that we are clinicians. I see patients and I like to see patients.

Listening to two lectures recently one of which was yours and the other from the director of what is called a medium secure unit in Britain, I had a fantasy which had to do with the period around the 1820s/40s when the first asylums were built. They were built in part because of public concern about dangerous lunatics at large in the community but this was allied with concern that there were people in jail who were more appropriately seen as being ill and in need of treatment. When the first asylums opened there were some who were keen or a moral/behavioural approach but others who felt that it was obvious that the conditions were medical and that we would only really have the answers when we had treatments that targetted the biological bases of the conditions. Very quickly however the demand for beds outstripped the supply and things began to fall apart.

Now recently in my clinical practice, I seem to be deluged with referrals of angry young men. It seems that there is some shift to seeing these problems as medical even though conventional diagnostic frameworks don't handle these cases very satisfactorily. In Britain a new generation of asylums seems to be

growing up, the medium secure units I've mentioned above and while these services were set up in the first instance for a restricted number of deluded criminals these other patients inevitably get referred to the forensic services and already demand greatly outstrips supply. Is this history repeating itself and will the cycle have to be as long this time or do you think we will have learnt anything from what we've been through.

Actually the first institution for mental patients based on a humanitarian approach was founded in Valencia in 1411 by a priest called Jofré, who after watching children in the streets throwing stones at a lunatic, preached in favour of such institutions the same day during Mass. At the end several merchants offered him the money for this institution under the condition that it should be run independently from the King, the nobles and the church. Before the end of the 15th century, several Spanish cities, Seville and Zaragoza, had hospitals and early in the 16th century, less than fifty years after Columbus first trip to America, the first hospital was built in Mexico City, two centuries before an institution of this kind was created in English-speaking America.

Now the boundaries between psychiatric and normal behaviour and deliquency and crime are not always clear and there is a group of individuals who create problems for both the health care system and the judicial and prison system. The fact that most prisons in developed countries provide the inmates with mental health care in a sense helps to solve this issue without confronting it. In Spain, now we are in the opposite situation; a new penal code takes a position against the discrimination against prisoners and transfers their care to the health care system. This creates confusion about the origin of dangerousness. All of this is forcing the psychiatric community to look for methods of care which will not transform every psychiatric unit into a high security unit and to differentiate the psychiatric and non-psychiatric aspects of aggressivity. In this context drugs of abuse are an important problem in parts of our country, especially against a background of high unemployment rates and a loss of traditional family values. My feeling is that in Spain we are going to follow the British model. Whether we will avoid an abuse of this or not I don't know. I think an external commision to supervise treatment and rehabilitation will be essential.