American College of Neuropsychopharmacology

Oral History of Neuropsychopharmacology

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Interviewed by Joel Braslow

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JB: I am Joel Braslow interviewing a distinguished colleague for the ACNP oral history series at our annual meeting in Hawaii on December 12. 2005. Please introduce yourself to our audience and the video camera.

JD: I'm José Manuel Rodriguez Delgado.* In Spain, you have a long, long name.

JB: Just tell me a little bit about your early childhood, where you grew up.

JD: I was born in Ronda in the south of Spain in Sevilla. Ronda was a beautiful town. We used to go there with my family for summer vacation in July and August. We had a really nice farm and I was born there. Then from there we went to Senegal in North Africa.

JB: Why were your parents in North Africa?

JD: My father was a major in the army and, we were fighting the Arabs, the Moors and the Muslims. We were in a beautiful place, in Helga. From there we went to Victoria in the Basque country and that's where I had my elementary schooling. Then I went to Madrid to get my MD degree and my doctorate in Science.

JB: When did you decide to become a physician and a scientist? And what made you decide to do that?

JD: I was in the third year of medical school when I started to do brain research with Professor Juan Negrin. Do you know Juan Negrin. He was the head of armaments during

* José Manuel Rodriguez Delgado was born in Ronda, Spain in 1915.

the time of the Republic. He was fighting Franco, and then the war was lost and he went to Mexico.

JB: After the Civil War?

JD: After the Civil War, in 1939, and he asked me to go with him to Mexico. I don't know whether I did right or wrong, but I wanted to stay in Spain. My problem was that Spain had no monkeys and I could not do my research without monkey brains. At that time, monkeys were not sold in Beijing or any of those countries.

JB: This was in 1939?

JD: No, I jumped in time. I am talking about 1940 or 1941. To solve my problem I went to Africa and brought about forty monkeys, two chimps and one gorilla back with me. At that time it was a long trip and took about two weeks. When I returned to Madrid, I asked myself, "what am I going to do? I'm going to do brain surgery on my gorilla? He's my best friend. I'm not going to do that."

JB: You became attached to the gorilla on the trip?

JD: Yes, and I decided to give the gorilla to the Madrid Zoological Company. Then I continued doing research on the other monkeys. But it was after the war, and I had no instruments to do research in Spain. Then I found out that in the United States there was intensive brain research going on, so I decided to go there. And I met Professor John Friedman, Major John Lilly and many other people and began to do research at Yale University in New Haven, Connecticut.

JB: When was that?

JD: That was about 1942 or 1943, and I stayed at Yale for twenty-two years.

JB: Till 1974, is that right?

JD: From 1942 to 1973, something like that. Those were happy years. Those were the years when most of my research was performed.

JB: So, let's go back in time. Before you went to Yale, you had been doing what sort of work?

JD: I was in Madrid, at the Ramón y Cajal Center. At that time, the Center was in El Rápido, a beautiful park in Madrid. I started to develop electrodes for brain implantation.

JB: What motivated you to do electrical stimulation of the brain?

JD: I thought the most interesting field in medicine was the brain and I wanted to know what was going on inside the brain. Implanted electrodes were first used in 1932 by Professor Hess in Switzerland in cats. But he used a primitive technique. I should not say that, because he was a Nobel Prize winner.

JB: He got the Nobel Prize in 1949, is that right?

JD: I think later. I continued that line of research. I improved the electrodes. Instead of one I had seven electrodes, which were left in for weeks, months and even years. I did that, fifty-five years ago.

JB: So, you continued that work at Yale.

JD: I continued in monkeys for seven or eight years. I was able to induce yawning, multiple behaviors, pupillary dilation, so then I decided, if it works in monkeys why not implant electrodes in humans? Now we are in 1952, in Providence, Rhode Island, where in collaboration with Dr. Hannibal Hamlin, a surgeon, we began implanting electrodes in schizophrenic patients.

JB: Was this done for the first time in 1952?

JD: Yes; it was the first time that electrodes were implanted in human beings.

JB: What were your thoughts about that?

JD: Remember, 1952 was the age of lobotomy for which Egas Moniz won the Nobel Prize. I was not happy with lobotomy and wanted to see what we could do with implanted electrodes in schizophrenics, epileptics and depressed patients. John Fulton did not win the Nobel Prize, but he was the author of important work on the structure of the brain.

JB: You were in his department. Is that right?

JD: I had a joint appointment in physiology and psychiatry, a full professor in both.

JB: You were not happy with the results of lobotomy?

JD: I was asked whether I wanted to do lobotomies and I said no, let’s wait until the methodology is improved. But, we had to treat epileptic, schizophrenic, and depressed patients.

JB: Treat them with what?

JD: With electrical stimulation, mainly frontal lobe stimulation.

JB: How did you do that? I mean, technically.

JD: It was necessary to make a little hole to place the electrodes steadfastly as possible into the brain, to stimulate it.

JB: How did you implant electrodes?

JD: The electrodes were implanted surgically.

JB: What did you find?

JD: In some patients it worked, in others it did not.

JD: Again, when did you do it for the first time?

JD: In Providence, Rhode Island in 1952.

JB: Was it done in a patient diagnosed with schizophrenia first?

JD: Yes, it was. And then, we did thirty-five or forty patients. In some of the cases we were very successful.

JB: Where did you implant the electrodes? Was it in the frontal lobes?

JD: In the frontal lobes and in the thalamus, mainly. We also implanted electrodes in the rostral part of the brain.

JB: Where in the rostral part of the brain?

JD: The septum and the head of the corpus callosum. These are the two areas with inhibitory functions, as demonstrated in monkeys, chimps, gorillas, sheep and many different varieties of animal. Then, I thought, if brain stimulation works so well with electricity we should try chemically. So I continued my research with chemoelectrodes. The chemoelectrodes were very small and had a very fine tubing that I used for injecting the chemicals. At that time we were working in monkeys, not in humans, and we were studying the effects of cocaine injected into the brain.

JB: And, this was in the mid 1950s?

JD: No, it was in the 1960s. I don’t like to use pills. What happens when you take a pill? It will go through your brain but also the liver, kidneys and the whole body. I think it is better to inject the drug where the drug has its effect, inside of the brain.

JB: In your original research with implanted electrodes were you thinking of doing it for therapeutic purposes or for fundamental research?

JD: At the beginning it was only for fundamental research. In one of our experiments we were using computers and found we could establish communication between the brain and the computer and back. We did that at Holloman Air Force Base in the chimpanzee.

It was really surprising. Through the computer, we established that each time an animal had electrical activity in the limbic system, the central gray matter was stimulated. And then, the chimp learned to inhibit electrical activity.

JB: It was like biofeedback.

JD: Exactly. I think we found something that could and should be used today.

JB: When was this work done?

JD: That was in the 1960s, quite a long time ago. We also used electromagnetic waves in chickens. That was extraordinary: It would modify the egg.

JB: What did it modify?

JD: The fertilized egg was modified. What happens with a pregnant woman? She has an embryo inside her tummy. The question was whether electromagnetic waves could modify the embryo in a woman? You cannot do experiments with embryos or pregnant women, but you could do it in chickens. We learned that by using electromagnetic waves the embryo could be affected. It could be damaged. This risk must be considered very seriously by legislators, by the government and by women themselves.

Then I moved from Yale back to Spain. I had a very nice invitation from the Minister of Education, Pilar del Castillo. She said, “You ought to come to Madrid. We’re building a new Medical School at Autonoma University and we need your intelligence, your capacity to organize things.” I responded, “ I’m very happy at Yale. I don’t want to go back to Spain now.” But then, I thought, I owe some duty to Spain, after all I am from there. When I told Yale I was invited back to Spain, they said, “We’ll give you anything you need, salary, instruments.” That went on for several months. Then I asked my wife, “What do you think?” And she responded, “ It would be interesting to go back, let’s go back to Spain.” So we went back and I became Director of the Department of Physiology at the Autonoma Medical School. Then after that, I moved to the Cajal Center. The Cajal Center was originally organized by Generalisimo Franco, and one of the professors at the Center was his son-in-law. That was a big problem because when the new government came after Franco, everybody at the Cajal Center was dismissed, even very good people, including myself.

JB: When was that?

JD: About ten or maybe, fifteen years ago. I said I have been productive in research for a long time, I should retire. But should I retire and do nothing? I decided I would continue doing something which is perhaps even more important than research, and that is thinking about research ethics, about the philosophical implications of implanting electrodes, injecting chemicals into the brain. What is the meaning of all this? What is the meaning of life? And what I'm doing now is even more important than what I have done in the past; I think about the ethical and philosophical implications of brain research, the implications of cloning.

JB: Did those thoughts enter your mind in the course of your career as well? You were obviously involved in some very fundamental work, looking at the relationship between the brain and behavior, and were using pretty invasive interventions over the last fifty years.

JD: That's right. But what is the meaning of all this? When you stimulate the brain, a nucleus of the brain, and get an inhibitory effect on behavior? Anything you do to the brain has behavioral implications, social implications, and philosophical implications. One needs to think about the implications of one's own research. What you're doing is modifying the chemistry of the brain. That's what all the pharmaceutical companies are trying to do, modify by chemicals brain functioning and behavior. All right, there's an anti-epileptic drug and it works. But should it not be possible to administer it more directly to a specific locus so that it would not have secondary effects? This should be the goal of the companies.

JB: Tell me about some of the philosophical and social implications.

JD: Take a terrorist. The terrorist could be a good father, a good person because his brain and behavior is normal in all but one aspect, destroying lives and property. Would it be ethical to modify the brain of a terrorist? Now, let us try to find out why the terrorist is a terrorist. He is a terrorist because he has been inculcated to become one. Could you be a terrorist? Sure you could, because you're a normal human being. We are dealing with a philosophical question. The brain is the material support of the mind. And what is the mind? Well, the mind is something that is supported by the brain. Take a computer or a videotape.

JG: The videotape is a nice analogy in that even understanding the mechanics, you're not likely to understand anything about the content on the videotape.

JD: Exactly.

JB: You've been in the press a lot over the course of your career, and as you were talking it made me think that perhaps you've been misunderstood in a certain way. Could we talk about that?

JD: It was not misunderstanding. It was a lack of understanding.

JB: Can you tell me how it affected your career?

JD: I was doing what most brain researchers are doing, just trying to see how the brain works.

JB: But not many researchers have ended up on the cover of the *New York Times*. On page one of the *New York Times*, is that right? What was that like, getting acclaim and notoriety for your research, and how did that affect your career?

JD: It affected it very little because I was totally concentrated on my work. I did not have time to think about the implications of brain research. I think the newer generation of investigators should do more thinking about the implications of their research.

JB: Am I correct when you say implications, you mean ethical, social and philosophical implications?

JD: I mean practical use of their research findings.

JB: You think that should shape what researchers do? I mean, in the sense of thinking about how the research is going to be used or not used?

JD: That's right. What is research? Research is to find out what is real, what is going on in the brain. The results of your thinking are limited by the functions of your neurons, the function of your amygdala. Neurons are very similar; in frogs, in cats, and in human beings. All species of animals have neurons. You modify cells and thinking becomes different. This is happening in mental illness. That's why we should investigate what is going on in the brain of schizophrenic and depressed patients.

JB: I'm thinking now as you're talking, and I'm wondering, in fifty years from now, what would you like people to remember about you? About your work?

JD: They should remember my discoveries, because it is in their discoveries that people are different.

JB: When you look over your career, what is the biggest discovery you think you've made?

JD: Probably the communication between the brain and the computer. Could we communicate with the brain without words? One of the great possibilities in the future is to communicate without words.

JB: I notice that your wife came along with you. She's been a part of your life for a long time. Can you tell me a little bit about her? I think she has been an important collaborator.

JD: My wife has been a very essential part of my life, not only personally, but scientifically.

JB: That's what I want to hear about.

JD: When I was writing a paper I thought was very good, and showed it to her, she would say, "It's a lousy paper." And then, without any scientific knowledge, she was able to correct it. So Caroline has played a great part not only in my personal life, but also in my scientific life. She has been a very powerful contributor intellectually to my research, and to some of my discoveries. I am very grateful to her. She has collaborated in my scientific accomplishments all through my life.

JB: How long have you been married?

JD: Forty, fifty, sixty years, don't ask me how long, because I'll give you the run around.

JB: We've covered a lot of ground. Is there any material you'd like to add?

JD: No, the main thing is the necessity of thinking about the dual possibilities of the brain.

JB: Are you working on a book?

JD: This is what I'm working on now.

JB: You wrote a very famous book in the late 1960s.

JD: It was on my research, but I think the ethical and philosophical aspects I'm involved with now are far more important.

JB: Is there anything you'd like to add? You were honored by Congress.

JD: Oh, yes.

JB: Can you tell me something about that?

JD: Well, that was very nice. A Senator from California, I can't recall his name now….

JB: It was Sam Farr.

JD: Thank you. Sam Farr. He was kind enough to propose me being honored for my research. Doing research is wonderful! But thinking about the implications of our findings is more important than anything else. And that is what we are missing today.

JB: Terrific. I really appreciate you taking the time. Obviously, you have done a lot to try to help us understand who we are.

JD: We hope we will learn even more about that.