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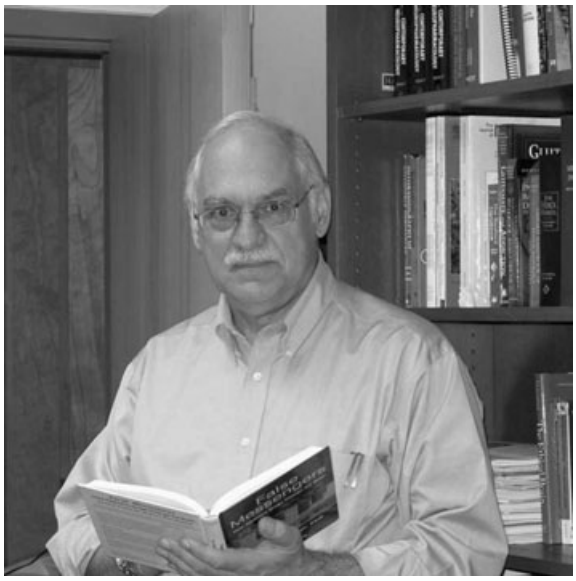
Conversation with Michael Kuhar



In this occasional series we record the views and personal experience of people who have especially contributed to the evolution of ideas in the journal's field of interest. Michael Kuhar is a brain scientist who has made astonishingly important and original contributions to the understanding of addiction.

Addiction (A): What forces in your early life directed you towards science?
Michael Kuhar (MK): My father, an electrician, was a big fan of science and math. I was always very good in math, and he encouraged that a lot. My mother suffered from depression, which got me interested in what is now called neuroscience.

'My mother suffered from depression, which got me interested . . .'

A: What can you recall about your mother's illness?
MK: She was very withdrawn. I recall my father's frustration, and her inability to do simple things sometimes. She was in the hospital where they gave her shock therapy, and it worked—but it frightened her so much that she wouldn't go back for it.

A: Where did you grow up?
MK: I grew up near Scranton, Pennsylvania, and went to college at the University of Scranton. I thought that I might go to graduate or professional school after college, so I didn't want to get into debt just then. The University of Scranton was local, reasonably priced and I had a part scholarship. So I went there.

A: Your college majors were physics and philosophy, an unusual combination for a student at a Jesuit school. Why that route?
MK: Sputnik, the Russian satellite, went up in about 1957, and that captured the imagination and excitement of my generation. Being good in math, and being from that era, I gravitated towards physics, as did many people. Philosophy as a co-major just somehow happened. I did like it.

A: When were you first drawn to pharmacology?
MK: Well, I first became drawn to biology in general in college, when I considered going to medical school. But I wasn't yet convinced that I wanted to make the change from physics to biology. In September 1965 I went to graduate school in physics, and that's when I decided that I wanted to go into biology. So I changed programs from physics to biophysics. I was drawn to pharmacology after that.

A: How long, then, did it take you to find biophysics?
MK: It took some months of searching around. I wanted to get into biology, preferably brain science, but I was in physics and I needed a link or a transition, and biophysics was a very reasonable transition. It was a very good department at Johns Hopkins, where I went as a graduate student in 1966. I loved the training there.

A: You went before long in the direction of pharmacology.
MK: I decided to study brain neurochemistry and neuropharmacology. I chose pharmacology for a very practical reason—I wanted to be able to get a job when I was done, and I thought pharmacology would be a more flexible degree than biophysics. Pharmacology opened the door to industry.

A: Who were your mentors at Hopkins?
MK: My first mentor was Dr Martin Larrabee, but my subsequent and main mentor was Dr Sol Snyder, who supervised my research at the hospital. When I first went to see the chairman of pharmacology, Paul Talalay, I said: 'I have no idea if you can help me, or if I should be here, but here's the direction I want to go in'. I talked about the brain, drugs and depression. And he said: 'we just hired the right person for you to work with, Sol Snyder'. And I said: 'who's he?'. He said that Sol was a bright young resident who was going to be an assistant

professor the next year. I was Sol Snyder's first graduate student.

A: What was it like to work with Sol in the early days of his career?
MK: He was relatively well known because he worked with Axelrod, who later won the Nobel Prize, but at that point Sol was still finding his way. He was a psychiatrist, so he was automatically studying the kinds of things that I was interested in. He was so good that he was promoted very rapidly from assistant professor to full professor.

A: So in those first days with him, what kinds of things did you work on?
MK: I was very excited to work on the uptake of neurotransmitters such as norepinephrine, GABA [gamma aminobutyric acid] and glutamate. I was excited about doing electron microscopy, so that I could see what the brain looked like.

A: What was your dissertation topic?
MK: It was one of several suggested by Sol Snyder, my advisor. Substances that were neurotransmitters had high-affinity uptake mechanisms in their nerve terminals. Sol said: 'you know, glutamate could be a major neurotransmitter. Why don't you look for a high-affinity uptake system?'. So I did, and I showed that if you took a slice of brain tissue and put it into a medium with glutamate the slice took up glutamate, and a highly disproportionate amount of it was found in nerve terminals in the tissue, suggesting a special nerve terminal uptake for glutamate as a neurotransmitter [1]. That, in 1969, was some beginning evidence that glutamate could be a neurotransmitter.

ENTERING INTO THE FIELD OF NEUROTRANSMITTERS

A: What did neuroscience look like when you were entering it?
MK: In my experience, which of course was limited, it looked like neuroanatomy, electromicroscopy, electrophysiology. Also, neuropharmacologists were experimenting, trying to improve antidepressants, and figure out better antipsychotic drugs and so forth. After I graduated from Hopkins, I went to Yale as a post-doc with George Aghajanian, who was working with LSD [lysergic acid diethylamide] and serotonin in the brain. I conducted a great deal of work on serotonin with George [2], partly because of its connection with LSD.

A: Who else was at Yale when you were doing your post-doc?
MK: Bob Roth, my other mentor at Yale, was more of a neurochemist than George, who was really an anatomist and electrophysiologist. Also my desk in my post-doc office was right next to George Paxinos. We used to discuss many things, including problems with early brain atlases—and with Watson, George went on to write the well-known atlas *The Rat Brain in Stereotaxic Coordinates* (Paxinos & Watson [3]).

A: When you returned to Hopkins as part of the neuropharmacology group, who did you join?
MK: It was me, Sol Snyder, Joe Coyle, and at times others. My laboratory work was a continuation of things I started at Yale. Before I left Yale, I conducted an experiment where I lesioned cholinergic cell bodies and showed that a high-affinity uptake for choline decreased [4]. Choline was the precursor for acetylcholine, and we had a novel situation where the precursor had a high-affinity uptake and not the transmitter itself. The transmitter was broken down by an enzyme, cholinesterase. So there was still a way to stop synaptic transmission for acetylcholine, which was to break down acetylcholine.

When I came back to Hopkins I continued studying choline uptake. I was focusing on cholinergic systems in the brain, and I made a little discovery—after I stimulated or depolarized cholinergic nerve terminals, choline uptake was increased [4,5]. The story that I proposed was that choline uptake—unlike the uptake for dopamine, norepinephrine or serotonin—was linked to impulse flow, which made sense because it was a precursor. The more the neuron fired, the more choline it needed to make acetylcholine.

'I was focusing on cholinergic systems in the brain, and I made a little discovery . . .'

A: Was that really your first breakthrough?
MK: As I remember, it was one that got me all excited; and it was probably my first unique contribution as an independent faculty member. Me and the post-doctoral fellow, Jay Simon, published the results in *Nature* [5].

A: When did you first get into autoradiography?
MK: I learned autoradiography with George Aghajanian at Yale. We showed that radioactive serotonin was taken up into nerve terminals by using autoradiography.

A: At that point in time, were there any particular neurotransmitter systems that were studied more than others?
MK: Well, many were studied. Norepinephrine was dominant in some circles because it was thought that the tricyclic antidepressants worked by inhibiting norepinephrine uptake. Now the emphasis is on serotonin and SSRIs [selective serotonin re-uptake inhibitors].

MOVING INTO AN INTEREST IN DRUGS OF ABUSE

A: When would you say that drugs of abuse become your main subject? What drew you to them?
MK: I was first interested in them as models for illnesses. For example, LSD produced psychotic effects and many thought that here is a model for psychosis. Amphetamine was interesting because, if you took amphetamine repeatedly, you looked like a paranoid schizophrenic. So I was interested in drugs that were abused from the perspective of their impact on the brain and the fact that they might be models for mental illnesses; but that evolved.

Bob Schuster and others showed that monkeys would self-administer drugs back in the 1960s and 1970s, and that almost all the drugs that humans abused were self-administered by monkeys. That seemed like a real breakthrough. It indicated that something innate in the brain wants you to take drugs. It isn't the devil or your mother-in-law, but an innate property of the brain that makes us (humans and animals) vulnerable to take these drugs. I was working on glutamate at the time, and there was the PCP [phencyclidine] issue which was related to glutamate, so drug abuse was interwoven into my scientific work. In the beginning I didn't focus on it as a special topic. That evolved over some years.

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A: At some point did you cross over to thinking that drug abuse itself was not a model for something else, but was something interesting in and of itself?
MK: Well, drug abuse is both a model and a field in itself. If you take antidepressants or antipsychotic drugs, you get a clinical effect that takes a long time to reach its maximum—weeks, maybe months. Everybody wondered, how is that happening? The drugs get into the brain in minutes to hours, but it takes days to weeks for the antidepressant effect or the antipsychotic effect to develop. That was a major mystery. Then it occurred to me, and I assume a lot of other people, that a model for this is addiction. An addicting drug gets into the brain quickly, but it takes a long time to get to the full addiction effect, and the advantage is that you can study addiction in a quantitative fashion. You can make animals addicted to opiates and give them naloxone and measure their reaction. The pharmacology of addicting substances was relatively well developed, so that was a major plus. So here we have a model where a drug takes a long time to get you fully addicted. Perhaps it's the same kind of thing that's going on when people are recovering from depression or psychosis. That led to my interest in drug addiction.

A: When do you think that insight dawned on you?
MK: Well, I think people had been discussing that problem. I would say I started thinking about that seriously in the early 1980s. To this day there are many people who work on both depression and addiction.

A: Back in the 1970s, when you returned to Hopkins, Sol Snyder and Candace Pert and others were involved in a race to identify opiate receptors. Can you describe what it was like there when you came back? Was there a difference in the atmosphere?

FROM AUTORADIOGRAPHY TO PET SCANNING

MK: Yes, it was a different place from the one where I had finished my degree. I was focusing on getting my own laboratory going, getting my own research going, but it was clear that Sol and Candace and other people were very excited over this binding data that suggested they had identified an opiate receptor. It was just tremendously exciting. I remember looking at some of the original data. They were using the 'grind and bind' approach, not autoradiography. The grind and bind approach was fast and effective, but provided only minimal anatomical information. Autoradiography with the light microscope gave much, much better anatomical resolution at the cellular level.

A: How were you using this technique?
MK: One of the projects I took on, as I had just learned autoradiography at Yale, was to try to localize drug receptors in the brain by autoradiography at the light microscopic level. This gradually skyrocketed. First, Sol and Hank Yamamura and other people showed that radioactive drugs could be injected into animals, and under certain conditions the drugs would be bound mainly to receptors *in vivo*. I carried out autoradiography on those brains where the drug was bound mainly to receptors.

Later a graduate student and I developed another more applicable and widely used autoradiographic technique, called *in vitro* labeling autoradiography. We used that name because the receptors in tissue sections, which were on slides, were labeled *in vitro* during incubations with radioactive drugs. This had significant advantages over the approach where animals were injected with a radioactive drug [6]. This technique is still important and used prominently today.

A: And these were brains of what organisms?
MK: I've mainly studied rats. Those first light microscopic studies of the autoradiography of receptors were very exciting. Being able to localize receptors in the intact brain by autoradiography at the light microscopic level was a precursor of PET [positron emission tomography] scanning. Because I had that experience, I knew exactly how to try to develop PET scanning for receptors.

'Being able to localize receptors in the intact brain by autoradiography at the light microscopic level was a precursor of PET [positron emission tomography] scanning.'

A: What did you learn from the autoradiography studies that you were able to transfer into the PET work?
MK: First of all, I knew that it was possible to inject drugs into animals under certain conditions and find times when most of the drug in the brain was on receptors. That's when you want to do PET scanning because you don't want to look at drug distribution, but you want to look at drug-labeled receptors so that you can localize the receptors. That's what I learned how to do with studies in rats. In rats I used it for cholinergic muscarinic receptors and opiate receptors. There were probably some others, but those were the main two. Carrying out that work, going through all the thinking and conducting a lot of experiments, even some that never worked, gave me the picture of how to do it.

A: When did you first hear about PET scanning?
MK: Somebody told Sol about it in the mid- to late 1970s, and Sol told me about it—at least I think that's how it happened. With the realization that you could localize receptors in the brain by PET, many radiologists or PET-oriented people became very interested. The importance of PET was that you could visualize the location and density of receptors in brain in living humans. It was not necessary to obtain brain tissue at autopsy and then assay the tissue for receptors by *in vitro* techniques. PET allowed the measurement of receptors after a simple injection and a brain scan. It was almost unbelievable. This approach could bring studies of receptors into the clinical realm, and it did.

Enter Henry Wagner, who was the head of nuclear medicine at Hopkins. He decided to bring a cyclotron and PET scanner to Hopkins and tackle the receptor imaging problem. He was a great guy, very jovial. Some thought he was not a basic scientist, but more of a clinician. Nevertheless, he was a visionary and he knew where he wanted to go. It's quite amazing that he held our group together for 5 years to write the grants, obtain the equipment, set up the equipment, build the laboratories and build the buildings. It took all that to get the PET scanning of receptors working. That's how long it took, about 5 years.

A: Wasn't that a huge investment at a time when the results must have been a little bit uncertain?
MK: Well, perhaps it was some misguided youthful enthusiasm but I knew, with reasonable certainty, that it was going to work. I knew how many receptors there were in the brain, and I knew how much radioactivity would be there if the receptors were labeled. The sensitivity of a PET scanner was known, and calculations showed that PET should be able to detect radiolabeled receptors. I remember saying that we have to get a drug-specific activity of 200 Curies per millimole or better. The radiochemistry people said: 'no problem, we get a thousand Curies per millimole regularly'. So I said: 'it's got to work'. We had a site visit, and I went over my calculations. I still don't know if any of them quite believed me and my colleagues.

A: Were those early studies actually dopamine receptors?
MK: Right, the first ones that we worked on were dopamine receptors.

A: Why were you interested in dopamine receptors?
MK: We happened to be working on them at the time. We thought they should make a very good imaging candidate because dopamine receptors are highly clustered in one place. Also, there were enough dopamine receptor ligands such that we could find one and methylate it, and it would still keep its properties. It needed to be methylated to add a carbon-11, which was a key for PET. Spiperone had a place where you could add a methyl group, which then became N-methylspiperone. That was the first dopamine receptor ligand we used. It's not used much any more. People have more selective and specific ones.

A: What was known about dopamine at the time?
MK: We knew antipsychotic drugs were dopamine receptor blockers. There were some ideas about amphetamine psychosis and dopamine; so dopamine was connected with psychosis back then.

A: Your 1983 Science *publication* [7] *was the first report of dopamine receptor imaging in human brain, and you had started becoming involved with PET in 1978, so it was 5 years from 1978 to that publication in 1983. You started working at NIDA in 1985. At what point did you see what you were doing with PET as working on the problem of drug addiction or drug abuse?*

MK: We thought PET could contribute to the problem of many illnesses: neurodegenerative diseases, psychiatric diseases, neurological diseases, behavioral disorders, all these things. We thought it was all wide open; and we could do it in people. Previously, we could not follow time courses of receptor binding in people, in parts of the brain, but now all that was within reach because of PET. It was like a fairy tale.

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A: How had you studied the human brain before this?
MK: We used human brains obtained at autopsy and conducted measurements with pieces of tissue. I had started my own brain bank, which amounted to a freezer with all kinds of tissues in it. You couldn't do that as easily now because of all of the appropriate, ethical and patient protection issues that have evolved, but we were able to obtain some tissue then. For example, we could call the medical examiner's office and ask if we could acquire any brains. They might say yes, I have an indigent person, and no one's going to claim the body, so you can have the brain. They respected the Hopkins researchers and it was sometimes just a phone call and a drive—but that was 30 years ago. The process would take more approvals now, and appropriately so.

A: Did you ever have brains of people who were known addicts?
MK: Yes we did.

A: Had you done work with non-human primates at that point?
MK: Yes, we studied some monkeys, just to be sure that receptor binding would work in primates. I had worked with non-human primates many years before that. When the opiate receptor was discovered one of my projects was to euthanize three monkeys, take out the brains and divide up the brain into many pieces and measure opiate receptors in all those pieces to see where the opiate receptors were concentrated [8]. Now, at that point I had not yet developed the autoradiographic technique, so measuring receptors required utilization of the 'grind and bind' approach.

A: How were relationships in the laboratory? Elsewhere you have described some difficulties with proper credit. In Sol Snyder's laboratory there was, of course, quite a controversy over that. What did you make of that?
MK: Well, we're all human beings and, unfortunately, less than perfect. That era, because of the conflicts, is one of the most difficult in my own personal memories. The opiate receptor was a big discovery, and people wanted their piece of the pie as they perceived it. The fighting for credit was sometimes bitter, and it only takes one or two people to create a lot of ill will. Sometimes the bitterness became destructive, bad decisions were made and there were accusations of misdeeds. I was accused of not giving someone proper credit—which was not true but nevertheless very painful. Accusations can easily injure reputations, and some people were very irresponsible. We gave significant technical help to colleagues who never acknowledged it, which was disappointing. Sometimes various claims were (and perhaps still are) made without documentation or support. Thinking about it, I can still feel wounded and disappointed, but I keep it in the past, which is where it should be. As human beings we are vulnerable to these things, but the discoveries were very important, couldn't be held back and fostered many positive advances.

MOVE TO THE ARC

A: Was that why you went over to the Addiction Research Center [ARC], which soon became the intramural research program of the National Institute on Drug Abuse [NIDA-IRP]?
MK: Mainly because of my desire to move ahead in my career and perhaps partly because of the distasteful political problems, I took the job at NIDA-IRP, which was just down the road from Hopkins. Dr Jerry Jaffe, the new director of the ARC and a 'mover and shaker' in the drug abuse field, offered me the opportunity to start a new Neuroscience Branch from scratch.

A: Why was the NIDA-IRP interested in starting a Neuroscience Branch in 1985?
MK: Jaffe thought he was opening up a new kind of research at the Addiction Research Center, and he was right. He was expanding the facility and bringing people together who could play a role in drug abuse research in the future. When I arrived there to create the branch, we pulled together some people who were already there. We had a group of about 15 people who were the beginnings of the Neuroscience Branch. At its height, after we recruited, it had about 85 people and half were PhDs. They then started taking parts of the Branch to found other groups and to give other people their own branches and so forth.

A: What were your priorities at the new Neuroscience Branch?

MK: One was trying to bring brain imaging to the ARC, to build up an imaging facility right there. Eventually we had a complete PET center directed by Eydie London. The other thing was to start up molecular biology. When I got to NIDA there was one person doing molecular biology. When I left there were more than 30 directed by George Uhl, so I feel that I met my major goals in my 10 years there.

A: What were you personally able to accomplish scientifically while at the Addiction Research Center?
MK: In terms of scientific accomplishments, one stands out. My laboratory published a paper in *Science* in 1987 showing that the dopamine transporter was the receptor for the addicting properties of cocaine [9]. The move to research on cocaine was partly political, in the sense that there was a great deal of money available for work on cocaine. Crack cocaine was being discovered and there was much interest in cocaine as an abused substance. An outstanding chemist colleague, Ivy Carroll, made hundreds of cocaine analogs that I tested in the hope of developing medications for cocaine addicts. We have a dozen patents, and one of those compounds is in clinical trials right now as a medication for cocaine addicts [10].

'My laboratory published a paper in *Science* in 1987 showing that the dopamine transporter was the receptor for the addicting properties of cocaine [9].'

A: How long did it take to get into clinical trials?
MK: Years and years.

A: Tell me more about the turn to molecular biology. Who or what forces were responsible for the emergence of molecular biology at NIDA?
MK: It may have been Avram Goldstein, a wise and accomplished scientist, who was on the board of advisors at ARC before I was there, and suggested that molecular biology should be a topic of research, and they hired someone. When I arrived at NIDA there was a lot more money, and that was an area that I chose to expand. Receptors were being cloned for the first time, and people were studying receptors in detail. Cloning and things like that were becoming part of everyday work in molecular research and drug addiction. We had to have it. We hired Dr George Uhl, who did a great job developing molecular biology and cloning the dopamine transporter [11].

A: Did drug addiction research at that point look cutting edge relative to other areas such as mental illness or alcoholism?
MK: For years I felt that research in drug abuse was in some ways ahead of research in other areas, because we were finding out the molecular sequelae of addiction faster than they were finding out the molecular sequelae of other diseases. Again, we have this very useful paradigm in which you can allow animals to self-administer drugs, and you can measure how addicted they are. We know when we've got something addicted. It is more difficult to know when we've got a depressed rat, for example.

MOVING TO EMORY

A: What kind of work did your 1995 move to Emory enable you to do?
MK: Well, I wanted to be back in a university because I liked the freedom and atmosphere. I moved to Emory at a time when the Human Genome Project was not completed, but was being developed. I thought it would be interesting to work on new genes involved in drug addiction. We didn't know how many genes there were then. I think it's very likely that we still don't know all the neurochemicals involved in drug addiction, so I kept looking at new genes involved in drug addiction as they arose. A group in Oregon published a paper on an mRNA that was increased when an animal was given cocaine [12]. The fact that the mRNA rose suggested that the product of that gene was in demand. It turned out that the product of the gene and the mRNA was a neuropeptide, cocaine and amphetamine regulated transcript (CART) peptide. It just happened to be discovered by addiction people. The name was just an accident of the circumstances of its discovery.

Some of the first studies that we conducted at Emory were on the anatomical distribution of CART peptide. In subsequent studies we showed that CART peptide is likely to be a modulator of cocaine's actions [13].

A: Were your new colleagues there interested in drug abuse?
MK: Yes, there were several people doing interesting work in the field. I added to the critical mass at Emory, although I never did accomplish as much as I wanted to at Emory, nor did I feel that I had the administrative or collegial support to do it. On the other hand, perhaps I could have done more myself.

A: Do you actually do non-human primate research?
MK: Sure. My interest is humans, and I'll use whatever model is required—primates or mice or cells in culture. I don't feel restricted to using primates here. Some of my earliest papers were on CART peptides in primates [14,15].

A: Has the CART neuropeptide continued to be one of your main foci?
MK: Yes. One of the first things we did with CART peptide was to look at the places where it was in the body. We were absolutely amazed to find that it existed throughout the body. It's not a minor thing found in just one piece of the brain. Judging from where it was in the body and in the brain, and this is where all my old anatomical training came in, it was clear that it was probably involved in feeding, drug addiction, endocrine control, stress, affective disorders and other things. We could look at where it was and guess that. Our laboratory was the first to propose that it was involved in feeding in 1997, which is now a major aspect about CART, which is involved in feelings of satiety. CART is not only an addiction peptide. It's something that evolution put there for many reasons [13].

A: Were you searching for medications that might treat cocaine abuse in your work with the Office of National Drug Control Policy [ONDCP]? What was the nature of that work?
MK: The work with ONDCP was a continuation of our work where we tried to find a substitute medication for cocaine. We were trying to find the methadone for cocaine. We used to playfully call it 'cocadone'. We have, as I told you, a substance in clinical trials that might be 'cocadone'.

A: Have you stayed involved with the clinical trial?
MK: I'm a consultant with the group that's doing the clinical trial on 'cocadone'. It is being funded by the NIH [National Institute of Health].

A: Have you developed any new scientific interests? Or is the CART thing really it right now?
MK: We're working on CART because every time we turn around there's something new and interesting turning up [13], so we have stayed with it. I'm also interested in mathematical modeling [16] and effects of maternal separation on drug use in offspring [17,18]—but we haven't yet been funded for that work.

A: Do you think that your most critical contributions will turn out to have to do with CART?
MK: No, I'm not sure what it will be or how that would be measured. Fortunately, my work is highly cited and that is very gratifying. My publications on transporters, receptor imaging by autoradiography and PET, cocaine analogs and CART peptides probably represent my main contributions. I also had some fun collaborations with other scientists on different projects.

I think of contributions or papers as each being a 'brick' in the 'wall of knowledge'. Each finding or publication is a new brick added to the top of the wall. Eventually the wall grows and grows, and our own bricks become further down as new workers and their new bricks of discovery are added on top of our own. After a while we can barely see our bricks down there lower in the wall, but they are nevertheless there and hold up and support all the new bricks that have been laid since. I've also become interested in ethics because ethics is evolving, and it's got a very good home in science. The ethical issues I'm particularly interested in include blacklisting [19,20], authorship and data management.

'I've also become interested in ethics because ethics is evolving, and it's got a very good home in science.'

A: Where do you see the field going, and how do you see the field evolving?
MK: First of all, I think brain imaging is going to play a major role in figuring out what's going on in the brain, even more so than it already has. I think that molecular genetics will help us to understand the vulnerability of certain individuals to drug abuse and what is the biochemistry of vulnerability, and that's going to go a long way. These are only my personal and subjective opinions. Other developments will have impact as well.

A: What do you think we will do with that understanding?
MK: We'll be able to predict who has increased risk of becoming a drug abuser. If a certain polymorphism of a certain gene confers a lot of vulnerability, we might be able to take that as a target for developing medications to blunt or reduce that vulnerability; but only about half the vulnerability is biological, and the rest is environment. If no drugs are available, you can't become an addict. If your parents took drugs, or if there are a lot of drugs in your environment, your vulnerability increases. If there is peer pressure, vulnerability increases. If you're from a broken home, vulnerability increases. There are many strong environmental factors, but there is something about the drugs that makes all species want them. Why do we take them? Because they take control over very powerful centers in our brain. That is the biological vulnerability. It is thought that, given the wide variation among people, that some people are much more vulnerable than others, or that the biological part of their vulnerability is more than others.

A: Tell us what you do when you have leisure time.
MH: Well, in my spare time I do photography, some of it competitive, and I am also a movie buff, which is sort of connected to my interest in photography. I sometimes enjoy the outdoors a lot—hiking, fishing and sightseeing.

I travel so much professionally that I am not someone who craves travel to faraway places. I enjoy discussion groups and my friends very much. If you peeked over my shoulder on a beach, you would find me reading popular mystery novels which I sometimes devour (and don't often admit). I usually spend holidays with my children and grandchildren who are, like all children and grandchildren, very special.

A: Any closing remarks?

MK: Well, I'm really glad that I had my opportunities and that I made the choices I did. Experiencing the discoveries changed me. While it wasn't always easy going, in retrospect it seems worth it. Also, I feel good about the younger generation of scientists who are very competent. It is a good feeling watching them develop into leaders in the field.

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