Mortimer Mishkin (NIMH 1955-current)

This is a second interview with Dr. Mortimer Mishkin, Chief of the Cognitive Neuroscience Section of the Neuropsychology Laboratory of the NIMH Intramural Research Program held on November 28th, 2001, in Bethesda, MD.

The interviewer is Dr. Ingrid Farreras of the NIH History Office.

Farreras: I'd like to thank you again for giving so freely of your time for this oral history. The last time we met you talked a little bit about your background – high school, your military experience, graduate school, your mentors, the type of research you did – and we stopped right after you joined Hal Rosvold at NIMH in 1955. At that time – NIMH had been established in '49 and NINDB in '50 – all of the intramural basic research for both institutes is reported in the *Annual Reports* together and [Seymour] Kety seemed to oversee both.

Mishkin: Yes.

Farreras: Was this because there was so much overlap in the subject matter?

Mishkin: I think it was the recognition that brain and behavior were so intimately linked that there wasn't any important difference between mental health and neurological health or mental diseases and neurological diseases.

Farreras: I remember reading that before they established NIMH there was some discussion over whether to call it the Neurological Institute or the Neuropsychiatric Institute, and there were political reasons behind why they finally settled for the name Mental Health.

Mishkin: Yes, and the political interests continued and resulted in ADAMHA [Alcohol, Drug Abuse and Mental Health Administration].

Farreras: Yes, I want to ask you about ADAMHA a little later. Why did the NIMH and NINDB split off then?

Mishkin: For political reasons. Not anything to do with science. That reminds me of something we talked about the last time. Congress dictates the institutes because it's the public, with its interest in various diseases, that puts pressure on Congress to do just that. If NIH had its way, there would be no such thing, necessarily, as institutes for particular diseases. It has nothing to do with science specifically; it has to do with the needs and the deep interest of the public and particularly those with family members who have various diseases which they want cured. And one way that they do that, and one way that Congress does not dictate but strongly encourages research in particular areas, is by simply devoting a certain amount of money to particular initiatives. With AIDS funds, for example, it wasn't necessarily a great idea because there was no good way to spend all of that money directly on AIDS research, so it was siphoned off to do basic research that was somehow, even if only distantly, related. And that's what happens often. There's this tension between Congress wanting to see the public's interests served and the scientists' need to study things that can be studied at that particular time where answers can be provided to certain questions but not others. So that tension is going to be present all the time. There's no way to eliminate it.

Farreras: Along that line of thought, would you say that, with that emphasis on particular diseases or disorders that the public focuses on and that Congress wants to allocate funding for, there was or is more of an emphasis toward clinical research versus basic research?

Mishkin: Yes, but I don't think that basic scientists at present, or during most of the time that I've been here, have felt that they haven't been well supported. But that's because, during that period, there was a tremendous growth in science here at NIH so it was possible to accommodate both clinical and basic research.

Again, I'm sure that there's always going to be some tension between the needs of people who are ill and what kind of science can be done that is useful, and you just can't attack it directly at the top. Or if you do, you find that you don't get very far, which is not to say that it doesn't spur some people to do things that they wouldn't otherwise have done and come out with important findings. On the one hand, the tension is inevitable. On the other hand, it's good, because good things – as well as bad things – do happen from the tension. But Congress doesn't tell scientists what to do.

Farreras: It doesn't dictate the research, just the institutes that are or need to be created..?

Mishkin: That's right. The institute is created, specific allocations are made for particular diseases…but on the whole, throughout research in this country, scientists generally do what they want to do. Unless they're in a pharmaceutical company or some other kind of private research institution.

Farreras: Were there any projects in your or other sections that were either aborted or had to be redirected or that the scientists couldn't pursue for any reasons? The proposals that I had just shown you from the *Annual Reports*, for example, were proposals which scientists submitted in order to conduct research. And then Shakow's report at the beginning was a summary of what research had been conducted throughout the year as a result of these funded proposals. So were there any that did not lead to subsequent research or had to be stopped…?

Mishkin: I'm sure there were, but it would be based on the decision of the scientists themselves or on the evaluation of outside reviewers, the Board of Scientific Counselors. I don't know when we started having outside reviewers – I'm not sure that they were present as early as '55 – but they were present soon afterward. Because however expert they [the Scientific Directors] may be in one area, they recognize that they are not experts in other areas, and so they cannot, by themselves, make those decisions. They have to depend on outside people to help. That's what the Board of Scientific Counselors is all about. They would review and evaluate the research and then advise the Scientific Directors of the institute, and as a result, there might be some changes in the direction of the research that was ongoing based on the productivity of the individual or of the lab. It always came down to how good the output was, so it relied on some evaluation by people who were considered to be knowledgeable, if not expert, in those areas. I'm sure mistakes are made. Peer review is terrible because it's always making mistakes, but we don't know anything better.

Farreras: Who was appointed to these boards and by what mechanism?

Mishkin: The recommendations come from the labs themselves, within the institute, but it's usually the selection of highly visible experts in the field.

Farreras: All of them non-NIH?

Mishkin: Yes.

Farreras: Do they have fixed terms?

Mishkin: I think so. Permanent members do, probably four or five years. And then there's the recognition that the permanent group of six, eight, even 10 members can't possibly know enough about what's going on in all of the different labs, so they have ad hoc reviewers as well, some of whom are suggested by the labs and others by the Scientific Director and his associates. They come in and help the permanent members on the particular lab that's going to be reviewed at that time. Increasingly, the evaluations depend on written records. They used to depend on oral presentations and lab and site visits, much like post grant-request visits in the extramural programs, but more and more we have these…you see that up there?

Farreras: The blue binder?

Mishkin: Yes. This is what the lab had to prepare for its last BSC review. It's huge! [3-4 inches thick] And people are supposed to read it! Of course, different ad hoc members are assigned different sections and so on but you get the picture. We never had to do this in the early years.

Farreras: Who has to write this up? Does every Section Chief summarize the work in his or her section and then send it to the Lab Chief to put together…?

Mishkin: Right. I'm trying to recall how it went in the distant past because that's what you'd be interested in. All I can think of is that we might have had short written reports. They might have been sent the latest summary of the <u>Annual Report</u> but they would probably evaluate the laboratory on the basis of the members' oral presentations and the record of research.

Farreras: You mean number of publications, presentations…that sort of thing?

Mishkin: Yes. It's a very difficult thing to do. In the end, it's almost impossible. Scientists have to do it historically, assess what has lasted and what hasn't.

Farreras: You mean assess productivity by looking at the long-term impact on the field?

Mishkin: Right.

Farreras: Is there any comparison with other standards, like academic standards? How do you obtain consensus on what is excellent or whether a lab's being productive?

Mishkin: Even consensus is a problem because consensus might occur too quickly and actually be inaccurate. It may shake out over a period of time, and what was thought by everybody to be fantastically good, can turn out to be nonsense. That may happen. The good thing that we can say about it is that it's a self-correcting process. Errors may persist a long time, but eventually they will be corrected. Science is fascinating as a group project.

Farreras: Yes, it is.

I also noticed that the *Annual Reports* would be divided into two parts. First Kety, for example, would provide a summary of the basic research conducted, with each individual lab subsequently reporting their work and then Bob Cohen would do the same for Clinical Investigations, with each of his areas reporting their work separately. But there were some years, between '61 and '66, when those two parts are combined and there's just one Joint Basic and Clinical Research. Do you know why they were combined during those years?

Mishkin: No, my suspicion is that it was a directive from above, either at the level of the Scientific Director or perhaps even the Institute Director. But it didn't mean a thing in terms of the content; that stayed the same. It was just packaged differently.

Farreras: And it didn't increase collaborations within the lab or with other labs..?

Mishkin: No. There has never been, to my knowledge, any successful directive to collaborate. Collaborations are generated by the individuals within the lab, within the institute, between institutes… They're individual scientist-driven, not directed from above. I don't mean to say that there may not have been attempts. Some of them might have even been successful in encouraging collaborations. But there has always been a notion that it would be good if there could be more direct collaboration between basic and clinical scientists, because the basic scientists are not familiar with the disease entities that the research ultimately hopes or serves to understand. And on the other hand, it is often the case that clinical scientists are medically trained rather than scientifically trained, and so they may not have at their fingertips the best kind of scientific techniques to use. But it's just very difficult to bring that about without the desire of the scientists themselves to do it, because they have their own agendas. The agenda can lead to collaboration but it isn't anything that you can dictate.

Farreras: Because if the NIMH was created in order to deal with all of these neuropsychiatric casualties from the war – given that there was very little knowledge about mental illness at the time – you would think that there would be an emphasis on starting off mostly with basic research in order to learn more about it before moving on to the treatment phase. But from the very beginning you can already see a division in the Lab between clinical and basic. But all the Section Chiefs were Ph.D.s, not M.D.s.

Mishkin: Right, in the Laboratory of Psychology. But there were other clinical laboratories that were also concerned with those diseases. When you talk about the need for basic research in view of the fact that we knew so little about the psychiatric disease entities themselves, I suppose the same thing can be said about absolutely every disease. And if the goal is understanding diseases, it's not a good idea simply to do basic research. So, as I said, I don't think that the tension is all bad. It's important to have both going on simultaneously. And there's always the hope – and it does happen in some cases, and we assume that it will happen in our case, too – that little by little, by which I mean over years and decades of research, and as we discover more, closer and closer collaboration will not only be desirable but possible and effective. And I think that that is actually something that we're seeing now. I think that the clinical research and the basic research are much more closely allied now than they ever were.

Farreras: You mean here at NIH specifically.

Mishkin: Yes, because of the development of the field. It could be partly because of changes in the personnel, but I think it's mostly changes in the field. There's a lot of recognition by the clinical people interested in depression, for example, that the work that has gone on in the study of the neurobiology of emotion is really important. But the work that has gone on in the neurobiology of emotion, as compared, say, to perception and memory and motor function, has been relatively little, and so the interest of the people in psychiatry and psychology on mood disorders and emotion and anxiety is actually helping to push more people to do that kind of basic research. So I think that area is going to grow – or continue to grow – and will be an area of significant interaction between basic and clinical. Of course, that's been going on for a long time in the field of cognition.

Farreras: You mentioned that most of the clinical people here are medically trained.

Mishkin: A lot of them.

Farreras: How much do you think that has influenced or is influencing the focus on a more biological or biochemical perspective to etiology and treatment?

Mishkin: Well, there was a recognition a long time ago that people who are medically trained also have to be trained in research. That's why the Howard Hughes Medical Institute is here on the NIH grounds. People who are medically trained and interested in doing research would do better if they had some background in science. And I think that is something that is already happening; a lot of the clinical people who are medically trained do have a lot of scientific background as well. But there was also a recognition that even the medically trained mental health people were not biological enough. So although biological psychiatry did get its start early, the kind of biological psychiatry that it was, was largely pharmacological, without a deep understanding of the neurobiology of the pharmacology. So there were an awful lot of drug studies. And maybe they were done well but it wasn't really neurobiology. It was a little bit more like chemistry than neurobiology. And that is what is changing little by little. The people who are interested in mental health are beginning to know a lot more about the brain than they did.

Farreras: Yes, that is one of the arguments used today against allowing prescription privileges to psychologists, by claiming that they don't know enough neurobiology to prescribe psychotropic medications.

Mishkin: That's a hard one. I suspect that there are a heck of a lot of psychologists who, on the contrary, do know a lot about the effects of drugs on the brain. But it is still the case that they're not medically trained. I'm sure it will continue to be a hard one to solve. I don't know if ever it'll be possible for psychologists to prescribe. We use the label psychology but psychology is a huge field. For example, just recently, in the National Academy of Sciences, there was a split between those who continue to be primarily experimentalists interested in the laws or principles of psychology, black-box psychology, and another group of almost equal number going off into what we refer to as systems neuroscience, which is one of the many labels that can be applied to the kind of neuroscience we do here in our lab. Integrative neuroscience is another term, cognitive and behavioral neuroscience is another term…but basically brain, behavior and mind. We're all psychologists, but I suspect that that division will continue even though we wish it didn't.

Farreras: And given the NAS's small sample size (of psychologists), I would expect to find more homogeneity – in terms of hardcore experimental psychologists – than I would within the huge field at large, where there are many more theoretical and methodological subdivisions and disparity in subject matter.

Mishkin: Well, this is science. Only scientists are elected to the Academy. There are many practitioners of psychology who would not be elected. There is nevertheless a trend which grows out of the emergence of new technologies like neuroimaging in which neuroscientists recognize the great value of research in cognition to help understand what is going on in the brain, and recognition on the part of the cognitive scientists, on the other hand, that they have important contributions to make and discoveries to be had by looking at brain function using their methods. So there are actually more cognitive scientists becoming interested in the brain and more interaction at that level than ever before, and I'm sure that development will continue.

And yet there will always be some level of scientific research in psychology that is too far removed from brain. Let's say issues in social psychology are raised for which brain function would be the wrong level of analysis. That may not be entirely true, but something like that is likely to continue for a long time. I say it may not be true because I think we increasingly recognize that brain is organized in such a way in mammals – and primates especially – that social interaction is actually one of the things that shapes brain functions evolutionarily and also dynamically.

Farreras: Are you at all concerned by technology dictating the questions we ask?

Mishkin: That always happens. But science depends on gathering converging evidence from different sources so the more techniques we use the better. Every single technique has problems, but every technique also has some advantages that no other technique has. So you try to make use of them. It's important, however, to recognize that we make mistakes because we sometimes draw conclusions based upon evidence gathered with a particular technique. One can see weaknesses and problems with different techniques or assessments so you have to use as many different approaches as you can, because no one measure of anything is really very good; it's always prone to error. And that applies to the different viewpoints that can be had by looking at a problem from different vantage points – basic versus clinical – as well. You have to understand, this is my personal philosophy.

Farreras: And it's very interesting!

Why don't you tell me a little bit about your work when you came here. You arrived in '55 to work in Hal Rosvold's Animal Behavior Section. What was some of the research that you were doing? Did you continue the temporal lobe research that you were doing with him at Yale?

Mishkin: Yes, and frontal lobe research. Those have been the major themes. But the work that we did in the early period did help lay the groundwork for systems neuroscience, and one way it did that was through the recognition that the visual system was something that extended beyond the primary visual area, or striate cortex. Lashley had argued from his findings that the only important area for vision per se was the striate cortex. We discovered otherwise. We discovered the relationship between what we referred to as the inferior temporal cortex and the striate cortex, and we demonstrated that the functions of the inferior temporal cortex depended upon the input that it received from the striate cortex – and that is one of the discoveries that led to the recognition that the so-called association areas of the brain were actually engaged in the processing of sensory information. We now think that this is the principle of organization of the entire brain, that different sensory modalities, with their inputs arising from the periphery and projecting to particular primary areas, are the source of processing streams that bring this information into areas that integrate and analyze the important stimulus features and bring it further into regions of the frontal lobe that are important for all kinds of higher mental processes. It's really great to think that we've made these advances over a period of 40-50 years. It wasn't anything that we thought about in advance. It was just that we had discovered that when we removed the inferior part of the temporal cortex bilaterally – this was what I had done for my Ph.D. thesis at Yale – we produced impairment in visual discrimination learning. And, strangely, it appeared to be modality-specific; that is, it didn't affect discrimination learning in other modalities, auditory or tactile… So how could that be? What is this area, so far removed from the striate cortex, doing having a selective relationship to vision? It seemed bizarre. And we had no good idea except that we then found some old anatomy – old Marchi fiber-stain studies by [Fred] Mettler – suggesting that there were anatomical projections from caudal (occipital lobe) areas in the brain to more rostral and ventral (temporal lobe) areas. And then we also found evidence from the strychnine neuronographic work of von Bonin, Bailey, McCulloch and others showing similar phenomena, evidence that there might be some interaction through neuronal connections between the occipital lobe and the temporal lobe. But no one ever understood what these fiber bundles were doing.

So I did this crossed-lesion disconnection experiment, the results of which allowed us to conclude that we could cut off the visual input to the inferior temporal cortex and produce the same impairment in visual discrimination learning as we had produced by removing the inferior temporal cortex, and that was a good discovery because it led us and others to do further neuroanatomical and neurobehavioral and neurophysiological work. In the end it led to this idea I think everybody accepts now, that there are sensory processing pathways or streams mediating perception in all the different modalities. That's not to say we know how perception works, but at least we know something about the neuroanatomical basis for it.

And we also know now – based on the work of a lot of other people – that each of these streams is made up of many different areas that receive the information, process it, and send it on in turn. All this happens very quickly; it just takes about 50 milliseconds for information from the striate cortex to get down, in the monkey, to the end of the inferior temporal cortex. That's not very long. But during that time, there's a lot of processing going on in all of these different areas within the stream that have to do with size and shape perception, texture perception, and color perception. We assume that all of this is being analyzed and integrated so that at the very end, based on work using single neuron recording, single neurons actually receive highly complicated information that allows them to respond to particular stimuli, like a face, anywhere in the visual field. It's an incredible thing. But we know only a little bit now about how it works, a little bit. The way in which the areas interact has now formed the basis for much of the research that is going on in perception.

Farreras: And that's what you and Rosvold were working on when you first arrived in the mid '50s.

Mishkin: Yes, that's what I was pushing. That was my work that we collaborated on. And then I collaborated with Hal on a lot of frontal lobe work because he was interested in the interaction between the frontal cortex and the caudate nucleus based on work that he had done at Yale with Delgado, after I left. Their stimulation work showed that they could interfere with delayed response by disrupting caudate function. Initially, they thought they were stimulating white matter; then they discovered that it was the caudate nucleus they were stimulating, and that, in turn, led to studies that were done here at NIH, and that we are still pursuing, on the interaction between the cortex and the caudate nucleus and other parts of the basal ganglia. That has also become a focal area of research because we think that this interaction is critical not just for motor function, as we know from Huntington's and Parkinson's diseases, which target the basal ganglia, but also for a form of learning that has been referred to in some cases as procedural learning – by us as habit learning – in contradistinction to another kind of memory which we refer to as cognitive memory, or others refer to as declarative memory. We knew from the clinical research literature (particularly the work of Brenda Milner) that the cognitive form of memory was served by the medial temporal lobe, and what we were able to show by following the sensory processing streams from vision was that an important area of output from the inferior temporal cortex was the medial temporal lobe, and it was work on the medial temporal lobe that led to the discovery that this was a critical station in the monkey for recognition memory. So these two areas of research that Hal and I worked on in the early '50s really paid off, both of them helping to lay the foundation for systems neuroscience.

There is no way that we could have imagined at that time that this work could have any direct relevance to mental health. We were only studying simple behavioral processes in the '50s. We were looking at discrimination learning and at spatial delayed-response, that one being a really simple test of where-did-I-hide-the-peanut, and trying to understand a little bit of the neural basis for these abilities. But uncovering the functional neuroanatomy that underpinned these simple abilities meant that we were looking at neural mechanisms that are absolutely basic to our understanding of mental function and mental disease.

But we didn't know what we were doing then other than following our noses in terms of those very simple questions.

If you now look at the literature on mental illness – schizophrenia, depression, obsessive-compulsive disorder, you name it – we're now talking in terms of brain circuits and systems. But at the time, we knew nothing about brain circuits and systems. We and others discovered them (always guided, consciously or not, by ideas like those of Hebb). And that is what has really opened up our understanding of higher mental function and disorders of higher mental function. We were basic scientists, but it did turn out to be valuable for clinical purposes, just as it was supposed to. My focus was on temporal lobe research and Hal's was mainly on frontal lobe research. But we worked together on both of them and now have a picture which emerged only very, very slowly out of that early work. It all has to do with brain systems and circuits.

So when someone asks me what my specialty is I usually say functional neuroanatomy. What we have also been trying to do now is to fit this functional anatomical story together with work on some of the neuromodulatory and neurotransmitter systems because we need to understand the neurochemistry and neuropharmacology. And so now we're looking at that aspect of neuroanatomy as well; that is, the relationship between the dopamine system and the cholinergic system and various kinds of learning and memory that we've been studying, and how these neuromodulatory systems interact with these brain circuits. It's also the case - because of the work that I'm doing in London, where so much of the interest is in children with brain injury who have various kinds of speech and language disorders – that we've extended our work here to the auditory system because we know so little about it. I was interested in what you gave me [photocopy of one of his *Annual Report* proposals from the mid 1950s regarding an auditory project] because most of our work was in vision, and the work in audition was not carried forward because it was so hard. It's still hard. It's difficult to train monkeys on complex auditory tasks. They're not good at them. And yet we do know that they have a lot of brain tissue devoted to auditory processing. A lot of the effort of my group now is in trying to build our understanding of the auditory system in the monkey, partly with the goal of trying to help think better and more clearly about speech and language, because we don't have any good functional neuraanatomy of that modality. And if we're going to make any good progress with this work on children – with their many speech and language disorders from various types of brain damage – then we really have to understand the functional neuroanatomy of audition and vocalization in the monkey. So that's what we're trying to do.

Farreras: I should have asked you this earlier, when you were talking about your graduate work, but why monkeys as your animal subjects, versus rats, mice, pigeons, snakes…?

Mishkin: Well, our interest was in higher mental functions and even though we didn't know where we would end up, the monkey, with its relatively large primate brain, seemed like a good model – better model than a rodent anyway – if we were ever to understand human behavior.

Farreras: For a closer generalization to human behavior…

Mishkin: Yes. And it was feasible at the time. God, if we were to start this now, I don't know if we would ever get it off the ground. At that time, the research was not that expensive. You may not understand this, but…

Farreras: Oh, yes, aren't monkeys about $4,000 each today?

Mishkin: More! They're getting to be $6,000 now! Do you know how much a monkey cost us at the time? $25. Perfect size, a young adult, an old juvenile, say about three, four, five years old. Perfect.

Farreras: What's the life span of a monkey?

Mishkin: About 30-35 years, a few might go on to 40, but not very much more. So it was feasible, it was practicable, even though it was relatively expensive compared, say, to pigeons or rats. God, I don't know if it would have been possible to start anything like that now, and young people at universities are having a hell of a lot of trouble doing so because of the expense. Yet I think we need more research on monkeys rather than less. We also need more research on apes. The ape is halfway between the monkey and the human, and there are human mental and brain processes that we will never be able to use the monkey to understand without going through the ape. The monkey brain is about one-sixteenth the size of a human brain. And the chimp brain is about one-fourth the size of a human brain, or about four times the size of a monkey brain, so it's right in the middle in terms of brain size. And my feeling is that we are desperately in need of studies of systems neuroscience – cognitive-behavioral neuroscience, integrative neuroscience, whatever you want to call it – in the chimp, which should be doable now if it were permitted, because it could be done noninvasively using neuroimaging techniques. So I think there's a possibility that this will get started.

Farreras: Here?

Mishkin: No, but somewhere like Yerkes [Regional Primate Research Center] where there already is a large chimp lab. It's a large primate research lab, which was moved from Orange Park, Florida – the lab I was telling you about last time – up to Emory [University] in Atlanta.

So we have looked at the visual system, somewhat at the somatosensory system, now increasingly at the auditory system, and we are trying to figure out the way in which the systems serve perception in those modalities, how they interact with the basal ganglia in order to serve what we refer to as habit learning, how they interact with the medial temporal lobe and the limbic system in order to understand what we refer to as cognitive memory, and how they interact with the frontal lobe to serve working memory, categorization processes, and reasoning.

Farreras: And these early results basically determined all of this functional neuroanatomical work you have done since then?

Mishkin: Yes.

Farreras: Was there anyone else in the Animal Behavior Section working with you and Hal on this research?

Mishkin: Hal, Al Mirsky, and me in the beginning. But after that, besides several post-docs, there were a couple of people who came into the section and were soon tenured…Josephine Semmes came in in the early '60s – and that was the start of the research on the somatosensory system, which was her interest from when she'd been in Orange Park. And a few years later, Patricia Goldman (now Goldman-Rakic) came and joined in the work on the frontal lobe, which then really took off.

There's a precursor to the work that I did on the temporal lobe, and that was the work that Karl Pribram did with Josephine Semmes and Chow at Orange Park. What they had done was remove bilaterally, in monkeys, all of the parietal, temporal, and occipital cortex outside the primary projection areas. So they left the striate cortex, the primary auditory cortex, and the primary somatosensory cortex, but they tried to take out everything else in the posterior part of the brain. And they studied discrimination learning in various modalities as well as some more complex processes like delayed response. Anyway, they found lots of impairments. They started to think about them in terms of somatosensory function in the posterior parietal lobe and possibly visual function in the temporal lobe, but they couldn't understand them at that time. And that's what I did my thesis on. It was based upon that earlier work that Karl and his colleagues had done at Orange Park. And the work that we did on the frontal lobe was a direct outgrowth of our work on lobotomized patients that I mentioned to you and the work that Jacobson had done earlier on chimps and monkeys in Fulton's laboratory, looking at delayed-response function. So there were important precursors to our work.

Another important precursor was the temporal lobectomy work of Heinrich Klüver and Paul Bucy at Chicago. One of the things that we set out to do was to make use of the work that had gone on in Orange Park and the temporal lobe work of Klüver and Bucy to try to see if we could fractionate – this is how we referred to it – the Klüver-Bucy syndrome. The Klüver-Bucy syndrome in monkeys is a very complex syndrome produced by bilateral temporal lobectomy and consisting of tameness, psychic blindness, hypermetamorphosis, dietary changes, hypersexuality; a whole range of symptoms which made up this complicated syndrome. And we did succeed in fractionating it. We found that the so-called psychic blindness was dependent, in part, on what we later discovered to be the occipito-temporal processing stream in vision. The interaction with the medial temporal lobe, particularly the hippocampal system, is what led to the so-called psychic blindness, that is, the inability to learn new things visually. The removal of the amygdala was particularly important for the production of the tameness or loss of fear in the monkey. So we fractionated that syndrome but, more importantly, we began to understand the circuitry.

The major organizational principle of our work initially was functional localization. But what it ended up being was a recognition of the organization of systems; that is, no area in the brain is an island unto itself. And I think that was the most significant aspect of our work, the recognition that the brain is made up of functional systems based on neuroanatomical connections.

Farreras: Incredible.

Did this work influence the subsequent development and expansion of the section into a lab, its own Laboratory of Neuropsychology?

Mishkin: I may have told you that Hebb's book is subtitled A Neuropsychological Theory. He was not *the* first, but he was one of the first to popularize the term neuropsychology. We were all deeply influenced by this book and the field was changing gradually from the use of the term physiological psychology, which is what we called it at that time, to neuropsychology.

Farreras: But the section wasn't called that at the beginning.

Mishkin: No. It was called Animal Behavior because that was the most important distinction between what we were doing and what others were doing.

Farreras: Others in the Laboratory of Psychology?

Mishkin: Yes, we were working with animals.

Farreras: Although Don Blough in the Perception and Learning Section experimented on pigeons. So, then, what brought about the name change to Section on Neuropsychology in '63?

Mishkin: I think it was the recognition that the most important thing that we were doing was not just working with animals but working on brain function in this area of psychology. And there were a lot of different labels that one could have applied but we chose this one because of our connection to Hebb. There was psychobiology, the term preferred by [Roger] Sperry. Psychophysiology was sort of taken over by people working, on the one hand, on the autonomic nervous system, and on the other hand, by people working with electrophysiology, event-related potentials (ERP), and so on. Physiological psychology was the term used for all of these types of research, but then the specialists began using separate terms, and now we call ourselves by still another name, neuroscientists.

Farreras: Yes, I noticed on your vitae that you use the term 'research psychologist' and then it's 'research physiologist'...

Mishkin: As a psychologist yourself, this is something you'll probably find interesting. That had to do with the fact that a psychologist could not get the salary that I was thought to merit at that time, and in order to get the promotion, I had to change from psychology to physiology. It had to do with federal standards and presumably with the issue of supply and demand of psychologists versus physiologists. This is something that you might want to look into.

Farreras: Yes, I'd be interested in learning more about this. So were physiologists more highly paid than psychologists?

Mishkin: Yes, and they could go to a higher level, too.

Farreras: So what did you have to do in order to become one or to switch from psychology to physiology?

Mishkin: Just change my title.

Farreras: Oh, that's it? No coursework or…

Mishkin: No, no. Because I was already doing physiology.

Farreras: And I imagine you couldn't have applied this retroactively?!

Mishkin: No, but this is something that you might be interested in following up on because it is clearly the case that psychologists were…

Farreras: At the bottom of the totem pole?

Mishkin: Yes.

Farreras: Who else or what other categories were available? We know there was a difference in salary among M.D.s and Ph.D.s, but…

Mishkin: And that is still true. M.D.s get a big bonus.

Farreras: Right. So among the different levels that were available there were psychologists, physiologists, psychiatrists…

Mishkin: Well, but then they would be M.D.s while a physiologist would be a Ph.D.…chemists, biochemists…

Farreras: So those were the three main groups? How did you learn about going about changing to physiology?

Mishkin: I don't know but I'm sure there must have been a heck of a lot more disciplines. The administration indicated that this what would have to happen for me to get the promotion.

Farreras: Okay. So you were just saying that you would attribute the Section name change from Animal Behavior to Neuropsychology to Hebb's book subtitle?

Mishkin: Well, no, Hebb's book came out [1949] long before we even came here. But by the time '63 rolled around we had been pushing for this for maybe a couple of years or so, and it was finally accepted.

Farreras: By “we” you mean Rosvold was behind the name change?

Mishkin: Yes, Rosvold and I.

Farreras: And once the name was changed were there any changes within the Section?

Mishkin: No, just the name changed. That was it.

Farreras: And then shortly after, in ’66, Shakow retired.

Mishkin: Yes.

Farreras: Was he still around after he retired or was he gone completely?

Mishkin: I think that he was sick – I’m not sure – but he was gone from the lab.

Farreras: But he didn’t die until ‘81?

Mishkin: Really?

Farreras: Yes.

Mishkin: Are you sure?

Farreras: Yes, are you thinking perhaps of John Eberhart, who went through several bouts of illness?

Mishkin: No, I had thought Shakow died a lot closer to the time he retired.

Farreras: And then David Rosenthal took over the Lab...

Mishkin: Yes.

Farreras: Although I hear he did so very reluctantly, that he didn’t want to be Lab Chief...

Mishkin: No, he didn’t.

Farreras: Al Mirsky seems to recall that the lab’s name changed from the Lab of Psychology to the Lab of Psychology and Psychopathology when Rosenthal took over. But according to the Telephone and Scientific Directories, that didn't happen until the mid-'70s.

Mishkin: Forget the Telephone Directories! They're always way behind.

Farreras: OK. What about the Scientific Directories?

Mishkin: Where would the Scientific Directory appear? In the Telephone Directory? Same thing. Way behind.

Farreras: No, it's a separate document with an annual bibliography included in it of what scientists had published that year.

Mishkin: It is?

Farreras: Yes, I can bring you a copy of one next time if you'd like to see one.

Mishkin: You mentioned Walter Stanley. Shortly before his Section ended I think he was not well.

Farreras: Yes, I understand he suffered a psychotic breakdown or something. But it was Rosenthal's idea to create this new Section on Comparative Behavior? I was under the impression that Rosenthal really sought to tighten or narrow the scope of the lab so that he wouldn't have to direct so much of it.

Mishkin: Was it his idea? I don't even remember that.

Farreras: I think so. What did this section do? When I think of comparative behavior, I usually think of animal research, too.

Mishkin: Yes. Walt Stanley would come to our lab and try to interact with us, but I don't recall what he was doing. I don't even know what animal he was working with.

Farreras: So aside from the name and Lab Chief change you don't remember any major changes occurring to or in the Lab?

Mishkin: No. Jim Birren had moved away.

Farreras: Yes, I'm not sure when he left for California.

Mishkin: That would have been a major change for the lab because he was an important figure.

Farreras: The Scientific Directory last mentions him in '64. That seems awfully early, even before Rosenthal took over.

Mishkin: But only a little while before. Yes, he might have left that early. Don Blough left for Providence fairly early; I don't think he was around very long.

Farreras: Yes, he was here from '54 to '58.

Mishkin: Is that all?

Farreras: Yes.

Mishkin: And Virgil Carlson, Ben Carlson, may have continued for some time, but he must have left in the late '60s.

Farreras: I have him listed here 'til '79.

Mishkin: Well, there was clearly an evolution over the entire period from the '60s to the '80s.

Farreras: And this is also around the time when NIMH was taken out of NIH and placed under ADAMHA, isn't it? That's the part we don't know anything about because those *Annual Reports* are missing.

Mishkin: Nothing much changed within the Intramural Research Program as a result of that.

Farreras: Do you know why it occurred in the first place? Who wanted it…

Mishkin: Felix.

Farreras: Felix wanted it out of NIH?

Mishkin: Wasn’t it Felix? When was Felix director?

Farreras: ’49-’64; he was the first one. But if the move was in the late 60s and early 70s I would have thought it had been under Stanley Yolles, who was director from ’64-’70…

Mishkin: I think it was Felix, who was a very effective spokesman for setting up mental health facilities around the country. That is what I think created ADAMHA. He got Congress to move on this pet project, and that resulted in the transfer of mental health out of NIH into ADAMHA. Because it became so heavily service oriented.

Farreras: ADAMHA.

Mishkin: Yes. That was the purpose. That was his goal. And there was, presumably, a terribly important national need that was being served. But, it didn’t really affect us very much in the Intramural Research Program. We continued doing what we were doing all along. That was the wonderful thing about NIH. We were protected from the science point of view. We kept our home here even though we were administratively separate.

I shouldn't say that it didn't make any difference. It may have interfered with the ability of the scientific director to keep NIMH space in NIH. I can at least imagine things like that happened.

Farreras: Was it just Building 10 and 9 that were used by NIMH?

Mishkin: There were other places NIMH had space in – 36, 15K… I imagine it must have been difficult at that time to keep things going, from a resource point of view, particularly physical space.

Farreras: But otherwise, everybody still went about conducting their own research?

Mishkin: Yes.

Farreras: Even though this was also the time, or shortly afterward, when the psychology sections sort of vanished? In the mid to late '70s?

Mishkin: Yes. I think the answer is that once the Section Chief went there was no reason for the particular research that that Section Chief was doing to continue.

Farreras: Were they staffed the same way they are now, where you basically have a Section Chief and then a few post-docs and some technicians, or were there other people of the same seniority as the Section Chief within the section?

Mishkin: The Section Chief usually had post-docs although there might have been a couple younger tenured people as in our section. One post-doc who became tenured while we were still a Section was Pat Goldman. I was tenured within about a year after I arrived.

Farreras: But your section was the only one that survived; it even became a separate lab.

Mishkin: Well, but the Laboratory of Psychology survived through different names; now it's Brain and Cognition.

Farreras: Right, the core of the Lab survived, but those original sections within it were gone for almost 20 years before the lab was renamed Lab of Brain and Cognition in the late 90s [under Leslie Ungerleider].

Mishkin: All but ours were gone?

Farreras: Yes, all of the sections except Neuropsychology seem to have disappeared by '74. The Lab was headed by Rosenthal from '66-'80 and by Mirsky from '80-'95. But since the sections seem to have disappeared by '74 it's as if Rosenthal and then Mirsky were heading a lab with no sections.

Mishkin: I see. All the others had disappeared by then.

Farreras: Except Animal Behavior, which later became Neuropsychology, which then became the Laboratory of Neuropsychology in 1977.

Mishkin: Well, in the end, we took over all of psychology at NIMH.

Farreras: Right! Well, maybe this is a good place to stop now and pick up with the Neuropsychology Lab the next time we meet. Thanks again.