

FEATURE REVIEW

Understanding the human brain: A lifetime of dedicated pursuit

Interview with Dr. Brenda Milner

Chenjie Xia

As a pioneer in the field of neuropsychology, Dr. Brenda Milner has contributed to many important landmark discoveries in the study of memory and temporal lobes, the lateralization of hemispheric function in language, as well as the role of frontal lobes in problem-solving. She is a fellow of the Royal Society (London) and the Royal Society of Canada, and a Foreign Associate of the National Academy of Sciences (USA). She has been recognized with numerous prestigious awards throughout her career, the latest of which include the Donald O. Hebb Distinguished Contribution Award in 2001, the Neuroscience Award from the United States National Academy of Science in 2004 and the Gairdner Award in 2005. Dr. Milner received her undergraduate degree at the University of Cambridge in 1939 and completed her PhD under the supervision of Dr. Donald Hebb at McGill University in 1952. She joined the Montreal Neurological Institute in 1950 to work with Dr. Wilder Penfield. Dr. Milner is presently the Dorothy J. Killam Professor of Psychology at the Montreal Neurological Institute and the Department of Neurology & Neurosurgery of McGill University.

I spent an afternoon with Dr. Milner on May 12th, 2006, where she shared with me her thoughts on her work, her perspective on the past and future of cognitive neuroscience, as well as her advice for students beginning in research.

How did you first become interested in science, and more specifically psychology?

Both of my parents were musicians. My father was a music critic and pianist, and he met my mother when she started taking singing lessons from him. Unlike my parents, it was soon apparent that I had no talent for

music. I did however have some interest in literature when I was young, which consoled them. In high school, I was always good at languages and my academic advisor suggested I go into humanities at Oxford. But as I loved mathematics and physics, I insisted on doing math despite everyone telling me I was foolish, and I managed to get a scholarship to study mathematics at Cambridge. That was in 1936, long before World War II.

When I got to Cambridge, I realized during my first year that I was never going to be a great mathematician. I believed, and I still believe, that you can always keep up with literature and languages on your own. Of course, it's different from doing a degree and taking classes, but you can do it if you are motivated enough. If you give up science however, you really give it up completely, because science is teamwork, which of course you really can't do by yourself. I suppose that was the reasoning behind what I ended up doing. Although I didn't stay in math, I still wanted to stay on that side, so to speak. So I thought maybe I'll do philosophy, since it is based on logic and I was a logical person. But then, everyone at Cambridge laughed at me and said, "Don't you have to earn your living? No one has ever earned a living in philosophy."

Nowadays, experimental psychology is grouped with natural sciences at Cambridge. However, before World War II, it was grouped with moral sciences, along with philosophy, logic and ethics. Thus, people around me suggested, "You shouldn't do philosophy, but have you thought about psychology?" And of course, I had not. Psychology had very little standing in England in those days, unlike in North America where it was more popular. I was given a big book to read over the summer and I decided to go into psychology. This was rather a

shock to my mother who had always hoped I would go into the arts side where she would then have been able to participate more in what I was doing. But she had reconciled herself to mathematics at Cambridge because it sounded pretty good. When I gave up mathematics to do psychology, I think she was really heartbroken.

So that was how I got into psychology. I knew I had to do very well, and I did do very well. I received a scholarship to stay on at Cambridge, which I suppose would be the equivalent of graduate studies in North America. Then, World War II broke out, and we were all put on to doing research for the Air Force. After my years on that scholarship, I worked in a radar research establishment, where I met my future husband Peter Milner, an electrical engineer. A couple of years later, in 1944, just as I was planning on going back to Cambridge to do more research, Peter was suddenly told that he was about to leave England with a group of physicists to go to Montreal, to help set up the beginning of Canadian atomic-energy research. When we arrived in Montreal, I had to get a job - I wouldn't have been happy not working. So I got my first job at the University of Montreal, where I taught animal behaviour and the experimental psychology of memory for several years.

How did you then end up working with Dr. Hebb at McGill? Did you have any particular reasons in choosing to do your PhD with him?

When we first came to Canada, the psychology department at McGill - and probably some other departments too - was pretty decrepit, since many people had left to do research for the war effort. In order to strengthen the department, McLeod, a distinguished experimental psychologist, was invited to act as chairman of the department. McLeod then recruited Donald Hebb who had previously spent two years at the Neuro¹ with Dr. Penfield and had published a few frontal-lobe cases before he went to study with Lashley in Orange Park, Florida.

I had realized by then that, in North America, you had to have a PhD to stay in academic life, which wasn't the case in England. It was at psychology seminars at McGill that I was attending where I first met Hebb. We were discussing the manuscript of his book *The Organization of Behaviour* and doing all the background reading. It was all very exciting. I was so impressed by Hebb that I decided to do my PhD with him. However, I had to persuade Hebb, because he wanted to be sure that I was serious, especially since I

was a woman. In those days, women would often follow their husbands wherever they went and be lost to science. Nevertheless, I convinced him that I was quite serious about it.

How did you come about working with Dr. Penfield?

When Hebb agreed to come to McGill, one of the conditions he insisted on was that Penfield accept one graduate student of Hebb's to study his patients. This was at the beginning of temporal-lobe operations for epilepsy, and Penfield was pioneering this surgery at the Neuro. At the time, not much was known about the function of the temporal lobes.

As Hebb's graduate student, I had first worked on tactile concept formation in the congenitally blind. I had established some relations with the Montreal Association for the Blind, and had started some experiments that interested me. It was then that Hebb suddenly asked if I would like to go to the Neuro to study Penfield's patients for my PhD. I accepted, started working with Penfield's patients in 1950, and became absolutely fascinated. When I finished my PhD in 1953, I wanted to continue working with Dr. Penfield. Hebb told me I was a fool. The early 50's were a hard time financially for most people, and since I held a tenured teaching position at the University of Montreal, Hebb thought I shouldn't give up such a solid job. Moreover, since he didn't speak French, I'm sure he also liked having his ideas taught in French. He told me I was a fool, and that no psychologist could survive for long at the Neuro. I said I would still like to give it a try. Although he really thought I was crazy, he still offered to support me for one year from his grants. So I left the University of Montreal and started working in the psychology department at McGill.

In the course of that year, Penfield and I saw two patients with severe memory impairment after their surgery. Before these two patients, I think Dr. Penfield genuinely thought he could be his own psychologist. He encouraged people to come and study his patients, but he thought psychology was just common sense and that he had plenty of it, which was true. When this memory impairment presented itself, things changed. You have to realize that temporal-lobe operations for epilepsy are elective. It's not the same as someone having a large brain tumour or vascular lesion, where you are trying to save their life. In that case, if the patients become paralyzed, lose their speech or memory, they are at least alive. It is different with epilepsy, and it really disastrous if your patients suffer serious memory loss. Penfield said to me, "You have to come to the Neuro, we need you!" I never thought the great Dr. Penfield would say "we need you." But he found me a little office close to the neurosurgical offices. And so, I

¹ At McGill, The Montreal Neurological Institute is commonly referred to as "the Neuro."

started working at the Neuro and have stayed there ever since.

Was HM one of these two patients with memory impairment?

No, not at all. This is something I have to repeat continually, because everyone seems to get it wrong. The first patients I saw with this memory problem were PB and FC, both of whom taught us a great deal.

In the early days when Penfield was beginning to operate on the temporal lobes for epilepsy, he was very cautious. In those days, you didn't know before going into the surgery what you were going to find. All you had was the plain X-ray films of the skull and a pneumoencephalogram where you would only see the size and shape of the ventricles. We also relied on the beginnings of EEG developed by Dr. Herbert Jasper, but EEG at that time were also very primitive. Before I arrived at the Neuro, Dr Penfield was confining the removal to the anterior temporal neocortex, and of course always to one side only. But as time went on, he realized that this neocortical excision was rarely controlling the epilepsy. The reason he had not touched the hippocampus up until that point was not because he had an intuition that it had something to do with memory, but rather because he thought that this huge, beautiful structure must be important, and why should you take it out if you don't have to. But as people returned from the surgery with their epilepsy still uncontrolled, he realized that he had to be prepared to take out the amygdala, part of the hippocampus, and some surrounding tissue from the medial temporal region. That was the state of affairs when I began working on my thesis.

PB was a civil engineer from the United States. He had had a neocortical removal from the left temporal-lobe in 1941, before I arrived at the Neuro. He came back about 10 years later still having seizures. So Dr. Penfield completed the temporal lobectomy, taking out the medial structures during the second surgery. The lateral structures had been removed during the first surgery. I tested PB extensively before and after the second surgery, as I was doing with all of Penfield's patients. I could show that, before surgery, this man's intelligence, as measured by the IQ test, was well above average, and his immediate memory span, his old memory and knowledge were all normal. But from the surgery onward, he was not remembering anything of everyday life. He would say to us, sarcastically, "What have you people done to my memory?" It was our first encounter with this peculiar memory impairment. Dr. Penfield, Dr. Jasper and I wondered what was going on. Penfield was of course very worried. Jasper, on the other hand, tried to reassure us, and said that there is

probably a peculiarity about this one patient that we didn't know about. A month later, we had another patient, FC, with the same result. FC was a glove-cutter and he had a one-stage left temporal lobectomy (including part of the hippocampus) and developed the same syndrome. At that point, Penfield and I speculated that this was the effect of a bilateral lesion, and that possibly unknown to us or misdiagnosed by us, there was more damage or atrophy in the hippocampal region of the opposite hemisphere, the right non-operated side. Thus, when Penfield removed the left hippocampus, he was effectively giving the patient a bilateral lesion. The emphasis on the hippocampus came from the fact that we only saw the impairment after the second procedure in PB, which involved only the medial structures of the left temporal-lobe.

We presented the data and this hypothesis at the American Neurological Association meeting in Chicago in 1954. After the meeting, Dr. Penfield got a phone call from a surgeon in Hartford, Connecticut, Dr. William Scoville. He said to Penfield that he had read our abstract with great interest and that he had seen the same result in a patient of his own after his operation. To put this in context, we have to go back in time into the bad old days of frontal lobotomies for schizophrenia. Scoville had carried out some of these operations and was not happy with the results. He had wondered if, in schizophrenics, it would help to do a bilateral medial temporal removal, because everybody was talking a great deal in those days about the connections between the medial temporal regions and the orbito-frontal cortex. He was a very good surgeon and he had developed an operation going in from the front and removing, depending on the patient, different parts and different degrees of the medial structures of both temporal lobes. This operation was different from Penfield's both in being bilateral and only medial, sparing the neocortex. Dr. Penfield used to say that it really fitted well with the Montreal operation almost as a planned experiment, since ours was a unilateral temporal lobectomy, and Scoville's operation was a bilateral medial excision and the common feature was the involvement of the medial structures. Scoville did this operation in different hospitals on patients with very severe schizophrenia, but he had not really followed them up. I studied some of his patients afterwards and found the same memory impairment in them, as far as it could be tested.

HM was not schizophrenic. He was a normal young man who had had very bad seizures from quite an early age, the etiology of which is not clear. It did not manifest itself as temporal-lobe epilepsy. He had many major convulsions and some absence attacks. He was on maximal doses of the anticonvulsant medications

available at the time. He was potentially of above average intelligence (as shown by postoperative testing), but was so obtunded from all these seizures that it took him many years to finish high school and he could not successfully hold a job afterwards. He was a desperate young man and had consulted Dr. Scoville for several years, seeking relief from his epilepsy. Although HM's epilepsy did not have a temporal-lobe origin, Scoville wondered if his temporal lobe surgery would be helpful, as he had become increasingly aware of the epileptogenic properties of the hippocampal region. This possibility was extensively discussed with HM, and eventually the operation was carried out. Actually, as far as the epilepsy was concerned, Scoville's judgement was right. Since the operation, HM had on average one big attack a year and a few small ones, and he is on considerably reduced medication. As mentioned earlier, Scoville had not followed up the schizophrenic patients, and suddenly this terrible memory impairment was obvious to him for the first time. Actually, Scoville published a paper in 1954, in the *Journal of Neurosurgery*, called "The Limbic Lobe in Man," in which he commented on this patient who "has lost his memory, but preserved the niceties of ward life", in that he was polite and knew how to behave, but couldn't learn his way to the bathroom and couldn't remember any of the hospital staff, except Scoville, whom he had known for many years.

When Scoville encountered our report, he called Dr. Penfield and suggested that we go and study his patients if we liked. So I started this really exciting period where I would go down by train to Hartford, work with HM for a few days and then come back to Montreal and think about what I had found. That was the beginning of the story of HM. He was not a Montreal patient, and Penfield never performed a bilateral medial temporal operation.

However, I should go back to PB for a moment. Penfield and I had speculated that there would be damage on the other side to account for the postoperative memory impairment. Years later, PB died of a pulmonary embolism. Penfield had maintained good relations with PB's wife and family and was able to carry out an autopsy on his brain, which confirmed that there was indeed atrophy of the right hippocampus, on the unoperated side, thus validating the hypothesis we had come up with to account for the memory loss.

Do you remember the moment when the idea of multi-system memory came to you? Was it an "aha" moment or did you have to think it through very carefully?

It was very much of an "aha" moment. I had met HM and had done all sorts of single-trial tests that

demonstrated the severity of his memory impairment. Then the question arose as to whether he could learn something new over multiple trials. So I went to the Introductory Psychology Lab of the Psychology Department, picked up a couple of tasks I could carry, and took the night-train for Hartford with my equipment. I suppose I chose good tasks: one was a maze task where you learn the path by trial and error; the other was a mirror-drawing task. Whereas HM made no progress with the maze, he showed good learning with the drawing task. It was a sensorimotor task, in which you are presented with a double-bordered five-pointed star and your goal is to trace a path that keeps within the two borders. The task would be extremely easy but for the fact that you only see the star and your hand as reflected through a mirror. This is difficult for anyone at the start, but with practice we improve, and so did HM. After three days of practice, his performance was perfect. He had really shown beautiful learning, although he had absolutely no awareness that he had ever done the task before. I then realized that this kind of learning is dependent on another system of the brain and I speculated that this applied to all kinds of motor learning. It was a very important breakthrough. To see that HM had learned the task perfectly but with absolutely no awareness that he had done it before was an amazing dissociation. If you want to know what was an exciting moment of my life, that was one.

How did you then make the jump to study interhemispheric specialization?

The interhemispheric specialization was not a jump. I started with interhemispheric specialization, not with memory. When I went to the Neuro to study Penfield's patients, I was trying to study the functions of the temporal lobes. But of course, since only one side was removed during the temporal lobectomy, in most patients (except PB and FC), there was a remaining functional temporal lobe. I compared groups of patients, the left (dominant) hemisphere group with the right hemisphere group. In those days, there was a strong neurological bias to speak of the dominant hemisphere, instead of language dominant as we say now. All good things were attributed to the left hemisphere. A very famous neurologist wrote about the dominant hemisphere and language with a very contemptuous dismissal of the other side.

I thought this was ridiculous, one of the reasons being that I had always been impressed by experimental work in psychology with monkeys. Monkey experiments can guide your work on the right hemisphere, but not the left hemisphere because monkeys can't talk. I was very much guided by the work with monkeys, which was beginning to show that there was an area in the temporal

lobe which seemed to be involved in complex visual memory. I remember Dr. Penfield looking at me in amazement and saying, "The temporal lobe is so far away from the visual cortex, why are you looking for visual effects there?" In those days, we didn't know about the ventral visual stream. I showed in my thesis that patients with right-temporal lesions (but not those with left) had difficulties with visual perception and memory, and that's essentially where my idea of complementary specialization of the two sides of the brain came from. Later on, I met Roger Sperry, from Caltech, who was studying patients on the west coast who had undergone cerebral commissurotomy, also for the relief of epilepsy. He invited me to visit him if I were interested in knowing what was happening on the right side of the falx. I accepted his invitation and studied various aspects of hemispheric specialization on his patients. So my work in this area pre-dated my work in memory and I would say that the notion of complementary specialization of the two sides of the human brain was a guiding theme throughout my career.

What role did your work on frontal lobes play in your career?

The frontal lobe was a funny story. When I first arrived at the Neuro, the frontal lobes were being debunked and were wildly unfashionable. Many extravagant claims had been made about them in the past, often based on bad data such as those from patients with huge tumours, or from lobotomies performed on severely schizophrenic patients. These studies were very tricky to interpret because they introduced many confounding factors.

We had far fewer patients with frontal lobe epilepsy than with temporal-lobe epilepsy, so we gathered the data slowly. I was following all the work going on in Wisconsin on bilateral frontal lesions in monkeys and was particularly interested by this difficulty the monkeys had with reversal learning, that is, the difficulty with learning one thing and then reversing to learn the opposite. David Grant was a very fine experimental psychologist working at the University of Wisconsin. He and one of his students invented the Wisconsin Card Sorting Task which was inspired by work with monkeys. I wrote to David Grant and told him I was interested in using this task with my frontal-lobe patients. He wrote back very enthusiastically and sent me the test materials. I collected very beautiful results demonstrating reversal-learning impairments in patients with dorsolateral frontal-lobe lesions, which were published in 1963.

During the two years Donald Hebb had worked with Penfield, the patients they saw had mainly been post-traumatic frontal-lobe cases. There was one famous

patient, KM, who was a workman in Nova Scotia. He sustained a very severe injury at work that destroyed one-third of both frontal lobes, similarly to Phineas Gage, and he developed post-traumatic epilepsy. He was sent to Penfield, and a bilateral frontal-lobe operation, which essentially consisted of cleaning up the lesion, was performed. Hebb studied KM pre- and post-operatively with a few basic intelligence tests and found no loss with the tests that were given. Hebb and Penfield both published very famous papers about the frontal lobes at this point, and Hebb became very skeptical of the importance of the frontal lobes for intelligent behaviour in the adult. He thought that maybe when you are growing up, you need the frontal lobes to develop your intelligence and skills, but once a certain level is reached, you are just running off your skills routinely - the frontal lobes playing only a minor role. Several other people, including the neurologist, Ritchie Russell in England, had adopted this view as well.

Years later, after I had published on card sorting in frontal patients, I got a chance to see this same patient, KM, on follow-up. He was no longer having seizures and I replicated all Hebb's findings on standard intelligence tests, but he failed completely on the Wisconsin Card Sorting Task. He showed the deficits that I predicted he would have, whereas he was fine on some of the memory tests that HM would fail. It was all very clear. But until the end of his days, Hebb could never quite assimilate this. In his capacity as my former thesis advisor, Hebb was often asked to write letters of recommendation for me for various reasons. When he wrote to me to bring him up to date on what I was doing, he would sometimes say, "Brenda, I think I know your temporal-lobe work very well. And I think you found out something about the frontal lobes, but I'm blessed if I can remember what it was!" I used to get cross about that; now it just makes me laugh.

So that was the beginning of the frontal-lobe story. Now, of course, the frontal lobes are everybody's love and I'm back in the temporal lobes.

Out of all your projects, which was your favourite part?

That's awfully difficult to say. Of course, the amnesia part has had the most impact. That's what I am sort of famous for, gotten awards for, and talk about more and more now because people like to hear the history.

I probably got the most kick out of the frontal patients. I like working with frontal-lobe patients very much. They do such unexpected things! I still remember this man with whom we were doing card sorting, the first category being colour, then shape, then number and so on. He was going on and on, failing the first category. And in my simple-minded way, I wondered whether he

was simply color-blind! But of course, he wasn't. It was just amazing to see someone whom you knew to be perfectly intelligent behave in such a way. This inability to regulate their behaviour by external cues is absolutely weird. I find it difficult to empathize with frontal-patients in this situation. Temporal-lobe patients forget - we all know what it's like to forget; it's a terrible handicap, but it's not actually a very interesting state of mind. It's much harder to understand what it is like being a frontal-lobe patient, so I am much more intrigued by it. They have lightened my life with the totally unexpected things they do.

How do you usually come up with a research idea?

The thing about me is that I am not a theoretician. I don't mean that I don't know other people's theories, I do read about others' work. But I'm not someone who comes up with great cognitive questions and then sees how I could answer them. I am extremely empirically driven. My quality is that I am a very good observer. I would note a funny little quirk in a patient and would think, "Well, that's interesting! Why did the patient do that?" and then try to figure how I could find out more about it and test it in a more scientific way.

I will give a small example. When I started working with left frontal-lobe patients, they were fine on their global intelligence, they weren't aphasic, and they were cooperative. But remarkably, they were lacking in spontaneous speech. I remember particularly this one young woman because she was very pleasant. She had a good IQ and including good verbal intelligence, but she was just not saying or writing very much. She even complained that her friends had stopped visiting her because, as she wasn't saying very much, they thought she didn't want to see them. I thought this was very interesting and that maybe frontal-lobe patients just weren't fluent, although their word-knowledge was fine; there is an important difference between word knowledge and word use. With that idea in mind, I started testing them with standard fluency measures. I was able to show clearly that these left-frontal patients had a deficit in word fluency. It is classic now; but back then, it was stimulated by observing that this cooperative and friendly woman was saying very little, despite having good verbal intelligence. It's something that strikes you and then makes you want to explore it further.

Throughout the early years when you worked with Dr. Hebb and then Dr. Penfield, how would you compare the field of experimental psychology back then to now?

As a discipline, I don't think experimental psychology was that different back then. There were scientific ways

of studying behaviour, and that was what psychology was about. Now, we have many more resources, especially in the last 15 years. We now have all this new technology such as neuroimaging. Structural MR was an enormous advance - those of us who are interested in looking at anatomical and physiological correlates of behaviour are able to do so now.

When you ask about psychology, you have to look at the impact of Hebb. Experimental psychology was a very well established discipline, with methods on how to analyze data, do statistics, and how to design experiments. I would say that was the same back then as it is now. But the idea of looking for the neural correlates of behaviour, the idea of putting those things together, what they now call cognitive neuroscience and what we called physiological psychology, was novel and was criticized by both sides. When Hebb wrote his book, he was criticized by some of the most senior and distinguished experimental psychologists of the day. They believed that we can do very scientific analyses of behaviour and make our own logical constructs to explain behaviour, but that when you start linking this to the brain, it's very premature. When you come to the side of medical people and physiologists, they were equally critical. They would say to Hebb that what he was doing was not physiology, but rather "physiologizing." By insisting on putting these two fields together, Hebb was a real innovator.

You were one of the first to bring together the fields of neurobiology and experimental psychology. You were also one of the first to integrate the clinical side into all this by studying lesion patients. What convinced you this was the right approach?

Well, I just loved it. Also, I was very lucky in that the psychology department at Cambridge, where I had studied before the war, always had a tradition that was very biological. We had to read a lot about the brain for our exams and so on. For example, if I had gone to London University, which also had a very good psychology department, I would have had an entirely quantitative psychology: intelligence; factor analysis; mathematical psychology. It would have been measurement, measurement, and measurement, with nothing about the brain. I think this is partly why Hebb chose me as his graduate student. I remember for our final exam at Cambridge, there was one exam of three-hour essay writing where we had a choice of six topics. I wrote on cortical localization of function, on sensory and motor systems, and a bit about language, because that was really all that was known. But it shows what we were trying to learn about at Cambridge in 1939. I think perhaps with this background, it was easier for me to assimilate Hebb's integrative approach than for some of the North American graduate students, where

psychology tended to be less biologically based.

I was considered very foolish to continue doing what I was doing. I'll make it a little bit of a caricature. It was supposed that, either you would take twenty rats through a learning study where you could do something physiological with the rats, or you would take twenty undergraduate students and perform some kind of psychology experiment on them. I, on the other hand, was taking experiments of nature. I couldn't just say, "Let's take these people's temporal lobe out." I had to take the patients as they came; I had to take them with whatever associated difficulties they had, their different degrees of epilepsy, and try to make sense of what was coming my way. People thought this was a foolish way to go, that it was better science to study the rats or the healthy undergraduate students than to study patients. Then, later, people said, "Well, you were so lucky." But I think I was just fascinated.

In a lot of your work, you were interested in lesion location linked with function. More and more work is now put into grouping different functions together into pathways and systems. If you had fifty more years, how would you take the work you have done up until now and integrate it into a system?

This is a very tricky thing, because I think it brings one back to the difference between functional brain imaging and the lesion method. You need both. With the lesion approach, you have someone who has had a permanent effect of this specific lesion, like HM, and you can know that the damaged structures were in some way critical to this kind of ability. With brain imaging, you can say that when this person is doing some kind of task, these areas light up. But you don't know which of these areas are really critical to the performance of the task and which are simply incidental. So you really need both approaches.

But of course, a much harder question is not that. The much harder challenge, which I have no answer to, is to put the molecular and the systems together. I certainly don't know how that is going to be worked out. It's not easy and it's not anything I'm going to contribute to, because I don't have the knowledge. It's not just because I'm 87, I could be 67 and it would be the same. I know a lot of younger people who are struggling with the same problem.

Do you think that the way we train very specialized researchers nowadays perpetuates the gap between the systems and the molecular?

Yes, I think it's a real problem. For example, when one attends a lecture on molecular topics which requires the knowledge that gene G58 does this or that, it's a whole new vocabulary that most behavioural scientists

just don't have. But I think it's a question of different temperaments as well. Some people feel very secure doing molecular work. I can remember the late Patricia Goldman saying that psychology was difficult, even though she was a distinguished psychologist. She retreated into molecular work because she found it easier. I think you have to look at the different kinds of brain and what comes easier to each of us. Certainly, one has to give beginning students in neuroscience more of a broad basis. But when the chips are down, you'll still find some people who like doing the molecular kind of research and some people who like doing the systems kind of research. There are going to be great people who can bridge the two, but it's not going to happen so quickly. But then again, I don't have a crystal ball, I'm not a prophet.

What do you think were the major changes that have occurred in the MNI over the past fifty years?

I think we have to say changes within the context of remarkable continuity. What is very special about the MNI is that Penfield's vision has been preserved in his successors, this wonderful bringing-together of people from so many cultures and backgrounds from all over the world, putting together the different clinical and scientific questions in the same house, same building; this remarkable family feeling is still here at the Neuro even though it has grown so big.

The big change was of course the bringing-in of the molecular. There was no molecular science at the Neuro in the old days. Even when people began to realize that the molecular was important, it was thought that that would be done at the Montreal General Hospital. The predecessor to the present director was actually brought in with the mandate to encourage the development of this whole side of neuroscience. Now of course, we have many molecular groups working at the Neuro, but you still have the challenge of getting the molecular and the behavioural groups talking to one another. Most of the scientists are still very much in one camp or the other.

What would you like to see in the next fifty years for behavioural neurosciences?

I really don't know, although I know which way it is going and it's not the way I would like to go. People now are looking at emotions, adolescence and social interactions, which one always felt were perhaps not very amenable to studying in the individual brain. This branch of psychology has never appealed to me personally, but I do think the field is moving that way with what I call these big fishing trips. They are beginning to think that they can ask questions or tackle issues that previous scientists thought not amenable to

the neuroscience approach.

How do you work with your students in coming up with a research project?

I've never given a student a specific project. I tell them what we are working on, I throw ideas onto them. Sometimes, they come back with things that don't quite work, but along the way, they find out what they are interested in.

For example, I wouldn't say, "I have this project written up in my grant for the CIHR and I'd like you to do the experiments." I would never do that. There's a real difference between being a research assistant and being a graduate student. When you've had your work and your projects considered worthy of funding by an agency and you've said to the granting agency that you are going to do these experiments, you hire a research assistant to help you do the experiments. That is a job. Graduate students are supposed to be learning what they are interested in. Obviously, if I am working in the field of learning and memory, and somebody comes along wanting to work on schizophrenia or emotions or something else, I tell them that I'm not the right person to be their supervisor. But if they are interested in the general area I'm working in, I expose them to everything that we are concerned in and the things we are tackling. Then, I ask them to do quite a bit of reading. They may come back with an idea that is not very well formulated and I can help them formulate it. But I am not going to tell them what experiments they should do. I know there are many supervisors who treat their graduate students as research assistants. I think this is unethical.

What qualities do you look for in your graduate students? What kind of skills do you encourage them to develop?

They have to have a lot of curiosity. Curiosity is what keeps me going at the age of 87. And there are a lot of other things. They must not have any illusions about science. They must not have any romantic notion that they are going to make a great discovery once a month or even once a year. There's an awful lot of routine in any job. You have to be willing to take a lot of measurements. You know that in molecular fields, you are doing a lot of boring bench work, but in this field too, you are doing a lot of routine work. For example, if you want to study spatial abilities or tactile modalities of patients with parietal lesions, you have to know about their thresholds for two-point discrimination. You have to take all kinds of very careful measurements of basic capacities before you can start speculating about higher functions. This can be very boring if you don't have the right attitude. I think people have to be very patient.

They also have to be ready to go into the lab. Hebb perhaps went to extremes that way. He really didn't encourage people to do all that much studying. He wanted them to be in the lab as soon as possible.

Another quality I look for in a graduate student is the ability to write. However, I think that you can learn to write and I've certainly taught people to write. I once had a student, a good student, who had always fancied herself as a literary person. She had taken many literary courses and wrote short stories. That kind of writing is fine, but it's not scientific writing. Not being able to write clearly is a big handicap, and I think writing clearly and thinking clearly are closely linked.

For students learning how to write scientifically, what advice would you give them?

Of course, you have to have someone who is willing to teach you and work with you. I have seen very good scientists who just don't care. I've read theses in which the experiments are good, but the writing just made my hair stand on end. The supervisor just didn't think it important, but it really is. I actually got that from Hebb - he really valued good writing. The really big thing is to anticipate your readers' needs. I remember working on my thesis. I prided myself on my writing and I remember giving Hebb the historical introduction to my thesis which I was quite proud of. He gave it back to me and said, "Can't understand it! Can't follow it!" I was so insulted; I didn't look at this thesis for about a month. And then I thought, "I'll show him!" I started realizing what the problem was. It was all there, but you have to anticipate your readers' needs. You have to tell them something in advance if they'll need it in the next paragraph. You mustn't tell them something at the end that they needed earlier on. You know these things, because it's your work and it's all in your head, but the poor reader doesn't have your head. This is absolutely a huge thing that people have to learn and then, it becomes second nature. After showing the second draft to Hebb, he said, "This is excellent, this would make a good article in the Psychological Bulletin," and it actually ended up being my first publication.

Chenjie Xia is a second-year medical student at McGill University (M.D. C.M. 2008). Her current research focuses on the roles of frontal lobes in affect regulation. She is the tenth Editor-in-Chief of the McGill Journal of Medicine.