John C. Liebeskind History of Pain Collection

Oral History Interview with Patrick Wall

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Biographical Sketch

Patrick David Wall was born in Nottingham, England, on April 5, 1925. He was educated at St. Paul's School, Christ Church College Oxford, and Middlesex Hospital Medical School, where he earned a Bachelor of Medicine in 1948. From 1948-1967, he held teaching positions in anatomy, physiology, and biology at Yale, the University of Chicago, Harvard, and the Massachusetts Institute of Technology; after earning his doctorate from Oxford in 1959, he was promoted to professor of physiology at MIT. In 1967, he returned to England as Professor of Anatomy at University College, London, and remained in that position until becoming emeritus in 1990. Dr. Wall is best known for his pathbreaking 1965 paper with Ronald Melzack ("Pain mechanisms: a new theory", *Science*, 1965, 150:971-979), which introduced the famous "gate control" theory; although modified and revised since, the theory remains a unifying concept of the pain studies field. He was a Fellow of the Royal College of Physicians (1984) and a Fellow of the Royal Society (1989). Dr. Wall was a founding member of the International Association for the Study of Pain (IASP) and served as editor of the journal, *Pain*. Dr. Wall died August 8, 2001.

See also: Obituary by Martin Koltzenburg in *The Guardian*, 16 August 2001
See also: Obituary in *The Times (London)*, 15 August 2001

Interview History

Dr. Wall was interviewed in his office in London by John Liebeskind on August 10, 1993. The interview lasted approximately 3.5 hours. The transcript was audit-edited by Marcia Meldrum and reviewed by Dr. Wall prior to its accession by the History of Pain Collection. The tape and transcript are in the public domain, by agreement with the oral author. The original recordings, consisting of three (3) 90-minute audiotapes, are in the Library holdings and are available under the regulations governing the use of permanent noncurrent records. Records relating to the interview are located in the offices of the History & Special Collections Division.

Topical Outline (Scope and Content Note)

The interview is organized chronologically with topical digressions, beginning with Wall's early education at St. Paul's and Oxford; his studies of brain physiology at Yale with H. T. Chang and Alex Morrow; his moves to Chicago and MIT with Warren McCulloch, and influential working relationships with Jerry Lettvin and Walter Pitts; experimental findings which contradicted the accepted specificity of nerve fibers and receptors; his collaboration with Ron Melzack; collaborations with William Sweet and Norman Shealy on stimulation analgesia; research in London with David Egger and Allan Basbaum and in Israel with Marshall Devor; Issaquah; Wall's interest in a pain journal and the role *Pain* has played in the field; his semi-retirement and present research interests. Major topics of interest include: the plasticity of the nervous system; the problems and methods of electrical recording from nerve cells; reductionism *v.* synthesis; the importance of patient observations in physiological research; development of the gate control

theory; Wall's view of the pain field; his iconoclasm; reminiscences of Warren McCulloch, Jerry Lettvin, and others.

Access to the Interview

This oral history interview, in its audio and transcript forms, is held by the History & Special Collections Division. Those wishing to use the printed transcript (which is available through Interlibrary Loan) or the audiocassette version (which is available by appointment only) should contact: History & Special Collections Division, Louise M. Darling Biomedical Library, UCLA, Los Angeles, California 90095-1798. Phone: (310) 825-6940.

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Citation Information

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Related Materials in the *John C. Liebeskind History of Pain Collection*

The researcher is referred to the following related materials: oral history interviews with Ronald Melzack and Ronald Dubner; organizational records on the journal *Pain* in the IASP Records (Manuscript Collection no. 124; Wall correspondence in the Willem Noordenbos Papers (Manuscript Collection no. 129).

Editorial Note

The interview transcript has been annotated -- with notes offset in [square brackets] -- to clarify and enhance the reader's understanding of the concepts and events described, but as sparsely as possible, so as not to interrupt the flow of the oral author's thoughts. By and large, the transcript is a record of the oral author's ideas and recollections in his own words.

Acknowledgments

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Patrick Wall, DM
(1925-2001)

Physiologist

PATRICK WALL INTERVIEW

TAPE ONE, SIDE ONE

JOHN LIEBESKIND: This is the beginning of our discussion with Pat Wall. It is the tenth of August, and we are talking about Dame Cicely Saunders [b. 1918, founder of the modern hospice movement].

PATRICK WALL: I'm just talking about the origin of the use of narcotics. In the sixties, in the minds of most doctors, narcotics were splendid for pain control, but because of the development of habituation would have a very short action. If you found people giving patients narcotics in rising doses over long periods of time, it was just assumed to be a polite way of killing the patients. What I was saying earlier on was that it was of considerable importance to have religious people start the hospice movement, because they were the one group that could not be said to be aiming to shorten their patients' lives. So Cicely Saunders may have started with some considerable trepidation -- after all, she had been through a regular medical school and had been told this was the way to kill patients if you keep it up, but she discovered that this was simply not the case. And she had lots of important students very early on, [Robert G.] Twycross [now Consultant Emeritus and Reader Emeritus in Clinical Medicine at Michael Sobell House in Oxford], Blount and so on, who developed the ideas, often in slightly different ways, which she was very willing to accept. She doesn't have a rigid pattern of what a hospice is supposed to be.

LIEBESKIND: Well, there was all this fuss about the cocktail, the Brompton cocktail [an analgesic mixture of morphine and alcohol in a flavored syrup, much used in British hospices in the early to mid-20th century], which I gather has changed.

WALL: Exactly, yes. And there, you see, you had a remnant of medieval medicine -- that is to say, polypharmacy where you just poured in mixtures of things, all of which were supposed to be good.

LIEBESKIND: I remember your editorial on this.

WALL: It is a denial of a sort of common sense, because you can't analyze the relative effects of the different compounds, and you assume that all patients need the same dose of things, even if they are taking two or three medicines, which obviously isn't true. So they set about analyzing the components of the Brompton cocktail, which contained narcotics plus cocaine plus alcohol and some flavoring. They simply went through these things one by one. It turned out that patients did not like the cocaine. Many patients don't like alcohol, and so on.

LIEBESKIND: Hard to believe, but true.

WALL: Not hard to believe in the sense of here are people hanging on and not liking to be confused, which is also what they don't like about narcotics, high-dose narcotics. She really is being honored. She has been put up very intensely for the Nobel Peace Prize.

LIEBESKIND: Has she really? Fantastic. Her title "Dame" indicates that that's some royal honor.

WALL: That's right. And somewhat more important, she has after her name "O.M.", which is the Order of Merit, which is the highest intellectual honor you can get in this country. There are only twenty-five of them, I think, so all the poets and writers and painters are in there with an O.M.

LIEBESKIND: She's already immortal.

WALL: Right. So that's a very rare honor here. So how have you thought -- do you have some sort of structured way? Well, go ahead.

LIEBESKIND: Although it will amuse you to note that I just tore the script up after about three seconds with John Loeser [Professor of Neurosurgery at the University of Washington, IASP President 1993-96], because he just pressed the talk button and it just keeps flowing. I have a set of questions, but they're overlapping and they're just sort of prompts to get you talking. I start with the question, just asking to go back to some of the beginnings, your education and so forth, what influences there might have been that you could document now, that you could recall, that led you towards the field of pain or toward physiology generally. Where did things begin?

WALL: Okay. So anybody who's been lucky has had a good teacher. I was fortunate enough to have two good teachers. One in school, which was the accident of the war, the accident being school teachers being called up into the army and people who for one reason or another couldn't go into the army being ordered to go to school to teach. So I was taught by a man called S. A. [Samuel Anthony] Barnett [1915-2003], who had just got his PhD in Oxford and therefore knew nothing about teaching, but a hell of a lot about science, and specifically about animals and animal behavior. So that was a great --

LIEBESKIND: This was school, in other words, before university. Where was this?

WALL: St. Paul's [in London, founded in 1509]. He became the world's great expert on rat behavior, field ecology and so on. He is now in Canberra at the Australian National University. [Barnett was Professor and Head of Zoology at ANU 1971-1980.]

LIEBESKIND: Do you keep in touch with him still?

WALL: Oh yes.

LIEBESKIND: He must be, what, in his eighties now?

WALL: Yeah. Right. And the second one was going to Oxford, and that was Paul Glees, a neuroanatomist [Glees (1909-1999), moved to Gottingen, Germany, in 1961 to head the Institute of Neuroanatomy and Embryology]. But there one should say the background to that. I'm talking now about 1945. And one has to realize that from 1850 to 1950, the nervous system was the great biological intellectual challenge. I don't think it was before, and I don't believe it is

now, unfortunately, but that meant that I was going to university and medical school where study of the nervous system was in general acceptable, including in medical school and specifically there, was the topic of interest.

LIEBESKIND: Why do you say that's no longer true? Now it's all molecular biology or something? Is that your thought?

WALL: Certainly. I would not automatically choose a group of people dealing with the nervous system for an interesting conversation now, and, well, I think one could go into that in depth. It seems to me horribly obvious. And of course, going back to Oxford at that time, it had been utterly dominated by [Charles Scott] Sherrington for practically a fifty-year period. [Sherrington (1857-1952), author of *The Integrative Action of the Nervous System* (1906), received the Nobel in 1932.) He was still just alive, but the effects were very strongly there. And of course he'd set off many schools, one of which was at Yale, with John Fulton [(1899-1960), Sterling Professor of Physiology at Yale until 1951), to which I went for my first job. So two spectacular teachers, both in a sense pointing at the nervous system. When I say spectacular teachers, I don't mean in any pedantic fashion -- I just meant they took some notice of me, which was so rare to have a teacher pay any attention to an individual pupil. That was what turned me on.

LIEBESKIND: I assume they admired your brain?

WALL: They were doing this in general to a lot of people, to people who made up a very devoted following. Also true that in Oxford, there was a chance to do research while being a medical student.

LIEBESKIND: You went for three years to regular university at Oxford and then into the medical, is that how that worked?

WALL: Right. Yes, here one actually starts at the beginning as a medical student. Here there's no initial course. That's supposed to have been done in high school.

LIEBESKIND: Which is then, what, a six- or seven-year program?

WALL: Yes, right. Fine. So that pointed me at the nervous system. And with this research experience, I had really already decided that although I would go through the procedure and finish medical school, obviously being interested in neurology and so on, that I would in fact be doing research.

LIEBESKIND: What research experience did you have at Oxford then? You said that it was possible there. What did you work on?

WALL: Right. So this was monkeys, thalamic interconnections, neuroanatomy, cortex to thalamus and so on. And I actually invented a lesion-maker which reappeared some twenty years later.

LIEBESKIND: Under someone else's patent.

WALL: That's right. And very simple, the problem was we knew electrolytic lesions were available at the time. Of course, at best you could only make a spherical lesion. I wondered how you could make lesions of other shapes. So I invented the idea of a bent wire coming out of a hypodermic needle which you could then rotate around and make cuts. The Hungarians reinvented that and have used it greatly in the hypothalamus.

So that was in fact my first paper, when I was aged twenty. Fine. So, just very briefly through the next stages. My first job was at Yale. I decided to go into physiology. Fulton, who was a pathological Anglophile and "Oxonophile" beyond that, was very good enough to take me -- I was an instructor, and in fact took over the job of Bob Livingston [Robert B. Livingston (1918-2002), son of William K. Livingston, later founded the Department of Neurosciences at the University of California San Diego], who had gone to Hess [Walter R. Hess (1881-1973), of the Physiological Institute at the University of Zurich, received the Nobel in 1949 for his studies of the diencephalon] in Zurich.

LIEBESKIND: So this was what, 1948?

WALL: Yeah. Fine. And there --

LIEBESKIND: Before we just continue too far forward -- is there anything even earlier, I mean, in your family that would have directed you towards science or medicine?

WALL: No. I come from an exceedingly liberal, supportive family who just said, "Go ahead."

LIEBESKIND: "Do whatever you like."

WALL: Right.

LIEBESKIND: Did you have other thoughts about careers at the time?

WALL: Well, of course, I assumed that I was going to be a normal clinician, and in fact I had --

LIEBESKIND: You knew you were heading towards medicine from even earlier.

WALL: Right. Yes, in fact, neurosurgery appeared to be something I might learn -- I took a brief fellowship in Sweden while a medical student and did a period in the Karolinska with Olivecrona, who was the world's great neurosurgeon of the time [Herbert Olivecrona (1891-1980) is considered the founder of Swedish neurosurgery], and I am deeply indebted to him because he cured me of neurosurgery. And already at that time I wandered off down the road to see [Bernhard] Frankenhaeuser [(1915-1994), leading Swedish neurophysiologist, author, with Andrew Huxley in 1964, of the equations describing the potentials of myelinated nerve fibers] and [Yngve] Zotterman [(1898-1982), Professor of Physiology at the Royal Veterinary College in Stockholm until 1963, a pioneering neurophysiologist and a leader in the field until his death] and these people, including [Ragnar] Granit [(1900-1991), Swedish neuroscientist who received the Nobel Prize in 1967 for his work on the physiology of vision].

Okay, so I turn up at Yale, where the resources and a large project had been set up, with a lot of people brought together at the same time to look at frontal lobes. This was because Fulton and Jacobsen [Carlyle F. Jacobsen (1902-1974), moved to SUNY Upstate Medical Center in 1950 and served as its first President, 1957-67) had operated on just two chimpanzees in the '30s and from which the whole frontal lobotomy epidemic spread. [Surgical ablation or severing of the frontal and prefrontal lobes of the brain to "cure" psychiatric patients was widespread in the US and some parts of Europe in the 1930s and 1940s.]

Fulton decided maybe it was a good idea to go back and have a look at the frontal lobes. And he quickly summoned, immediately after the war, a large group of people there, including [Karl] Pribram [(b.1919), innovative Austrian-born physiologist and psychological researcher, now Distinguished Professor Emeritus of Cognitive Sciences at Georgetown University], [Paul] McLean [later head of the Laboratory of Brain Evolution and Behavior at the National Institute of Mental Health], Rossner and many people. The Hartford place was just down the road.

LIEBESKIND: The Institute for Living [The Institute of Living in Hartford, Connecticut, is a mental health research and clinical center founded in 1822; Pribram was director of research there while he was at Yale].

WALL: Right -- where Weiskrantz [Lawrence Weiskrantz is now Emeritus Professor of Psychology at Oxford University] was just beginning and so on. So very, very good for discussions of the brain in general, [but] even for the time, curiously old-fashioned physiology, almost no electrophysiology going on. David Lloyd had been there but had already moved to the Rockefeller [Lloyd (1911-1985), spent much of his career at the Rockefeller, making detailed functional maps of the lumbar cord and afferent neural pathways], and had left behind him two people -- one was H.T. Chang, now in Shanghai [at the Brain Research Institute there], who was doing electrophysiology, and really I looked with wonder and astonishment at this, and he really taught me the beginnings. Another was a quite remarkable fellow called Alex Mauro [1921-1989], who came from electrical engineering, really a biophysicist, went on to the Rockefeller -- they all went on to the Rockefeller. So Chang taught me electrophysiology.

LIEBESKIND: He was doing single neuron recording at this time?

WALL: It was still general Lloyd-type recording. Mauro and I had a very good time together, and we started then with buried stimulators, radio stimulators, which he took on later for heart pacemakers, and so we had a paper in '49 or '50, "Cortical Stimulation in Monkeys" -- radio cortical stimulation -- which we used for various things and which I was to use again fifteen years later with the same gadgetry for peripheral nerve stimulation and cord stimulation. So while there at Yale, I came under the spell of Warren McCulloch. [Warren Sturgis McCulloch (1898-1969) was at MIT from 1952. He is perhaps best known for the paper, "A Logical Calculus Immanent in Nervous Activity", co-authored with Walter Pitts (*Bulletin of Mathematical Biophysics* 5 (1943): 115-133). This paper is widely credited with being a seminal contribution to neural network theory, the theory of automata, the theory of computation, and cybernetics.] And because of that --

LIEBESKIND: So you got to MIT [the Massachusetts Institute of Technology in Cambridge]?

WALL: Right, but by way of Chicago.

LIEBESKIND: That's looking ahead. So McCulloch was on the faculty of Yale at that time?

WALL: No, McCulloch at that time had moved from Yale to University of Illinois, where there was a very distinguished collection of brain people and in fact Chicago in 1950 was a hugely -- I would say that it was the American center of nerve studies at the time, because starting from the top there were people like [Percival] Bailey [(1892-1973, neurosurgeon who developed a classification of the brain tumors) and [Gerhardt] von Bonin [neuroanatomist (1890 -1979)] – [Horace W.] Magoun [(1907-1991), neuroanatomist most famous for his studies of the reticular formation] had just left, [Stephen W.] Ranson [1880-1942, pioneer in hypothalamic research] had, I think, just died.

LIEBESKIND: [Ralph W.] Gerard [(1900-1974), physiologist of wide-ranging interests, introduced the intracellular recording capillary microelectrode]?

WALL: Gerard was working away very hard. [Stephen L.] Polyak [(1889-1955), Croatian neuro-opthalmologist best known for his studies of the visual system] was there. And of course Roger Sperry [(1913-1974), Nobel Laureate 1981 for his studies of the differential functions of the two hemispheres of the brain] and Paul Weiss [(1898-1989), developmental and neurobiologist, originally from Austria]. So it was a quite extraordinary center, although falling to bits by the time I got there, but had been enormously important. So McCulloch in fact organized for me to be assistant professor of anatomy at the University of Chicago.

LIEBESKIND: So he was at Chicago?

WALL: He was at Illinois actually.

LIEBESKIND: The University of Illinois, Chicago Circle, or whatever it's called there?

WALL: Right.

LIEBESKIND: So you didn't know him at Yale at all. He wasn't at Yale.

WALL: No. He had been. McCulloch had worked at Yale in the '30s and early '40s with [Joannes Gregarius] Dusser de Barenne [(1885-1940) Dutch neurophysiologist, at Yale from 1930, who used strychnine to study the functional subdivisions of the sensory cortex] on strychnine neuronography, and a lot of things had come out of that.

LIEBESKIND: I gather he was quite a genius. Is he still alive, Warren McCulloch?

WALL: No. He was a genius at getting people together and getting discussions going -- that was no doubt about that. But of the people he'd brought together and succored, there were two people to be tremendously important to me. One was Jerry Lettvin and the other was Walter

Pitts. [Lettvin (1920?-), who trained as a physician, spent his career at MIT and is now Professor Emeritus of Electrical Engineering and Computer Science; Walter Pitts (1923-1969), was a brilliant but neurotic logician and cognitive psychologist, eccentric and socially isolated, who never earned a degree, but worked and often lived with McCulloch or Lettvin from 1942 until his death.]

So, to jump three years, the four of us, McCulloch, Lettvin, Pitts, and I, then migrated to MIT, where Pitts already was and had been with [Norbert] Wiener [Wiener (1894-1964), mathematician and philosopher, at MIT from 1919, is considered the founder of cybernetics].

LIEBESKIND: Was this the first of biology there of any distinction?

WALL: Oh no. MIT's biology goes back to the last century, with two things.

LIEBESKIND: Really. I had no knowledge of that.

WALL: One of course was [Louis] Agassiz [(1807-1873), Swiss-born biologist and paleontologist, at Harvard from 1848] and that group up the road at Harvard. Of course they were fascinated with evolution and comparative zoology. The Department of Biology carried out the first controlled study of canning -- how much you had to heat things and how to seal the lid. Canning had been used for a century -- in the Napoleonic wars they used tinned meat -- and it was great stuff except for botulinum poisoning and things of that variety. So, yes, they'd got quite a background in biology and long before I got there, F. O. Schmitt [Francis O. Schmitt, 1903-1995] had been the head of biology and he was an important character in his way in a number of things. He certainly played an important part in the beginning of electron microscopy and various other sorts of biophysics.

LIEBESKIND: The Schmitt trigger.

WALL: I think that's another Schmitt [Otto H. Schmitt (1914-1998)].

LIEBESKIND: Oh, is it really? I assumed that was --

WALL: Yes -- I'm not even certain that that Schmitt doesn't have two T's in his name. Yes. That was the Schmitt who worked with [Bernard] Katz [German-born neurophysiologist (1911-2003), at University College London from 1952, Nobel Laureate 1970]. In fact, our migration to MIT had little or nothing to do with MIT's biology. It was a quite different thing. Let me take the University of Chicago, or the Chicago part, because Lettvin and I got together. I had already examined the effects of strychnine, which was the first proper physiological recording experiment that I did, and had found that what McCulloch had been saying was simply wrong. So Lettvin and I got together to start looking at single units in the spinal cord and to question all the things that were happening in spinal cord at that time with the various dominating people, Lloyd, Eccles, the whole Sherrington school, and so on, that we had all sorts of reasons to doubt. We would have a "Fuck Eccles" week and then we'd have a "Fuck Lloyd" week. [John Carew Eccles had just moved from New Zealand to his native Australia, to the Australian National

University in Canberra. His pioneering work on the biophysics of synaptic transmission would earn him the Nobel Prize in 1963.]

LIEBESKIND: He was terribly amusing, was he not -- Jerry Lettvin -- a very comic fellow? I met him a couple of times, years ago.

WALL: Oh yes. And remembering that, at the time, quite extraordinary techniques were becoming available.

LIEBESKIND: This is now, what -- '50?

WALL: Yes, '50 to '53. Microelectrodes were available and we could play with those for the first time.

LIEBESKIND: Pipettes?

WALL: Pipettes and metal electrodes and so on. As important, electronics were under control and for that a very important addition for me was Frank Offner, a very remarkable chap, still alive and booming [Franklin F. Offner, 1911-1999].

LIEBESKIND: Really? The amplifiers?

WALL: Right. Offner had an electrical engineering degree from Cornell, then got a master's degree in x-ray crystallography with [Linus] Pauling [(1901-1994), Double Nobel Prizewinner (Chemistry 1954, Peace 1962), at the California Institute of Technology 1922-64], then went to the University of Chicago to get a Ph.D. in physiology with Gerard

And there's a very important paper, Offner, Weinberg and Young (Offner F, Weinberg A and Young G. Nerve conduction theory: some mathematical consequences of Bernstein's model. *Bulletin of Mathematical Biophysics* 2 (1940): 89–103), which really precedes certainly, Hodgkin and Huxley and K. C. Cole. [British researchers Alan L. Hodgkin (1914-1998) and Andrew F. Huxley (1917-) shared the Nobel Prize with Eccles in 1963 for their studies of the giant squid axon and 1952 equations describing membrane conductance (A quantitative description of membrane current and its application to conduction and excitation in nerve. *Journal of Physiology* 117 (1952): 500-544. American scientist Kenneth S. "Kacy" Cole (1900-1984) conducted experiments on membrane conductance with H. J. Curtis in 1939 and was Hodgkin's instructor in squid dissection.]

Any rate, he was utterly misused at the University of Chicago. They just said, "Oh, here's an electrical engineer, we'll get him to fix all the gadgetry." So he was used as a technician while being an immensely clever fellow, who then said, "Well, hell, if that's what academe is, I'll go off and found my own company." He says, and I can well believe him, that he invented the word electronics. Certainly there was a company called Offner Electronics by 1939. And he made several fortunes with electronics, part in industry -- but he always kept a finger in physiology and neurology - rather like Grass.

LIEBESKIND: I was going to say, he and Grass must have had rather parallel careers [Electrical engineer Albert M. Grass [1910-1935] and his scientist wife, Ellen Robinson Grass [1914-2001], founded the Grass Instrument Company in Quincy, Massachusetts, in 1935; the company is a leader in the manufacture of electroencephalographs and other neuroscientific instruments].

WALL: Oh, very much so, in things with medical and research uses. So it was an immensely exciting time technically because instead of sitting around talking about what nerve cells were doing, it became remarkably easy to record from them. So actually starting there in Illinois and in fact working, because Jerry Lettvin was getting his Boards in psychiatry and for that had to be a duty doctor in Manteno State Hospital [a psychiatric hospital in Illinois, operational 1929-85] -- he set up a lab, and I used to go and work there. Jerry would put himself on permanent nights and would work throughout the day and at night as well. Already at that time we were putting microelectrodes into spinal cord and did the first field plots of volleys entering the spinal cord.

LIEBESKIND: You were stimulating peripheral nerves with strychnine or electrically?

WALL: Actually, roots electrically, and following the waves going in. And this was just at the time that we were moving from Chicago to Boston. So that by 1955, by which time we were well in Boston, we had published what is in fact a stunning paper which showed presynaptic inhibition. [Howland B, Lettvin JY, McCulloch WS, Pitts W, and Wall PD. Reflex inhibition by dorsal root interaction. *Journal of Neurophysiology* 18 (1955): 1-17.]

LIEBESKIND: Really.

WALL: But presynaptic inhibition which included blockade of impulse transmission down the axons. So here were two unknowns, or three, four or five unknowns, saying that two things which had not been considered by the classics were taking place. One was presynaptic inhibition and the other was that impulses didn't run reliably down axons. And you can imagine that we were in trouble.

And an extraordinary event occurred for me. There was an international physiology conference in Montreal. And I was summoned into what amounted to a Star Chamber, which consisted of [Wilder] Penfield [1891-1976], [Herbert] Jasper [1906-1999], [Edgar] Adrian [(1889-1977), shared the 1932 Nobel Prize with Sherrington], and [John Carew] Eccles [1903-1997], all sitting in one room. [These four men might reasonably have been considered the deans of neurophysiology in the early 1950s.] They'd heard this report and read the abstract. And they in effect said to me, "Look here, you're obviously a decent chap with a good background. You ought to watch out what you're doing."

LIEBESKIND: Oh boy.

WALL: And that was essentially the interview.

LIEBESKIND: How did you feel about that?

WALL: Very, very bad.

LIEBESKIND: You were, what, in your late twenties at this time?

WALL: Yeah.

LIEBESKIND: It must have been frightening.

WALL: So in fact -- and there was then a five-year period from '55 to '60 when we were struggling to identify the components of this effect. At that stage we split in a friendly fashion in that Lettvin and friends went off looking at the visual system and the frog colliculus and so on, for which I guess they're most famous. [Lettvin JY, Maturana HR, McCulloch WS and Pitts WH. What the frog's eye tells the frog's brain. *Proceedings of the Institute of Radio Engineers* 47 (1959): 1940-1951.]

And I stuck with the spinal cord, and developed various ways of looking at this, this being how nerve impulses penetrate the cord and what the problems are and so on. The techniques were then very widely adopted, especially by Eccles, who then discovered presynaptic inhibition and primary afferent depolarization, without a whisper of this previous episode, needless to say. Any rate -- just again let me set the scene at MIT -- because we had not been invited at all by the biologists at MIT. We had been invited by the mathematicians and electrical engineers, and this was under the domination of Wiener, Norbert Wiener.

LIEBESKIND: Not Schmitt, who was in biology.

WALL: Nothing to do with him, and in fact quite antagonistic -- and Jerry Wiesner [Jerome B. Wiesner, (1915-1994), electrical engineer and science policy advisor]-- and the two reasons there -- one was cybernetics -- from Norbert Wiener's point of view, we experimentalists were just there to show that cybernetics, the details of cybernetics, were true. Pitts had in fact written quite a bit of the book *Cybernetics*. The other influence was the whole fascination with communications. [Claude] Shannon [(1916-2001), mathematician and developer of modern information theory] was there.

LIEBESKIND: [Walter] Rosenblith [(1913-2001), Viennese-born engineer and biophysicist who pioneered in the use of computers and mathematical models to study the brain]?

WALL: Rosenblith and so on. We'd all been brought in together with the idea that the brain was a supercommunicator, and while they were looking at radiowaves and such things, why not have a look at nerve impulses as well? So the intellectual background was in fact partly the mathematics of cybernetics and control, and partly this whole communication question on a very subtle level. There were some very, very bright people there.

LIEBESKIND: And was there a good community? Were there a lot of discussions and lectures and so forth?

WALL: Excellent.

LIEBESKIND: Well, it sounds like that was true for you really from Yale on forward.

WALL: True, true, but it was getting better and better. And so it was rich intellectually, plus all the technical possibilities. All these things that we knew we wanted to do, like averaging, became easy electronically, and so on, and we didn't have to worry about electrodes and amplifiers. They all worked. And there was enough money to buy the gadgets, not that we were expensive by comparison with what other people were doing.

Now this is by the way, and nothing to do really with the intellectual development. At MIT [in 1955] there was an explosion related to F. O. Schmitt, who was fired by MIT, one of those rare occasions where visiting committees recommend that the chairman should be parked on one side. And a new group came in -- a rather junior, very good organizer, not distinguished scientist called Irwin Sizer [1910-1990] took over from Schmitt, and this very smart Yankee decided that he was going to import and hire everybody a lot smarter than he was.

LIEBESKIND: He had good taste.

WALL: Right. And he set about making the quite remarkable faculty which is on now, starting with [molecular biologists Salvador] Luria [(1912-1991) Italian-born microbiologist and member of the original "phage group"] and [Cyrus] Levinthal [(1922-1990), author of "Levinthal's paradox'] and so on, who obviously led the whole molecular genetic, etc., business. And by good luck he chose me as his executive officer, so that for ten years or so, I was in with biology and able to bring some of the biology in.

LIEBESKIND: This was as Schmitt left and this fellow took over, you went over into the biology part of it.

WALL: That's right. And later on in that period there was another revolution in which Psychology, which had been going down to very little, appointed [Hans-Lukas] Teuber [(1916-1977), German-born neuropsychologist] and [Walle J. H.] Nauta [(1916-1994), Dutch/Indonesian-born neuroscientist who developed crucial methods of tracing nerve fibers in the brain] and so on.

LIEBESKIND: Don Marquis [Donald G. Marquis, physiological psychologist, later at Yale]?

WALL: Marquis had actually been there before. And that included Melzack, who was in with that transition.

LIEBESKIND: This was when?

WALL: Now we're talking about '62 or something like that. Okay, so that was the background of some interest in general about a tilt towards looking at the nervous system by new people and old disciplines looking at it in a new way, such as psychologists, which is very much what you were involved in.

LIEBESKIND: What was it like just personally? I mean, you were now an emigre -- you had been in the United States for twelve years or so.

WALL: Right. So, having left Britain in '48, married in '50, an English girl, but really never all that happy socially in the States, although having a marvelous intellectual time, and as time went by -- I should say, by the way, one of the other groups that was incorporated in this extraordinary group, all to do with communications, were the speech people, and that included [Noam] Chomsky [b. 1928, leading linguistic theorist and political critic] and [Morris] Halle [b. 1923 in Latvia, Professor Emeritus of Linguistics and Philosophy]. They were brought in more by engineers than by anybody else.

LIEBESKIND: That really became the seminal center for linguistics.

WALL: That's right. But again with the background of looking at phonemes and noise and so on. So it meant that, just in my own mind, I certainly didn't feel settled as an American, although I was obviously being splendidly spoiled; I felt remaining loyalties here.

LIEBESKIND: You still had your family here.

WALL: True, true. Aging parents and so on.

LIEBESKIND: Brothers and sisters?

WALL: One brother who was also off wandering the world, so that my parents were by themselves. And right from school, I had been far left-wing politically. I had been a member of the Communist Party until the late '40s. I actually split over [The Soviet Union's dominance of] Czechoslovakia somewhat earlier than most people, who split over Hungary -- I had a row over that, which didn't stop me. [they laugh]

LIEBESKIND: That wasn't very comfortable for you intellectually in the States, to be there at that time, a rotten time.

WALL: Exactly. The [Joseph] McCarthy period [McCarthy, an American senator, led an anti-Communist movement in the early 1950s, in which many people lost their jobs and were otherwise persecuted for even slight associations with Communism], and then Vietnam, and so there were a number of reasons why I had kept an ear and eye out for a job here. And in '67 I was offered a job here at University College [London], and moved on with very considerable trepidation, as you can imagine.

LIEBESKIND: From the standpoint of research support, and so forth.

WALL: Right. The work that I was doing, and still am doing, is relatively simple in terms of technical support and technical gadgetry, which helped considerably. An interesting small thing which made a very big difference -- there are still here technicians in the laboratories.

LIEBESKIND: That are paid for by the school.

WALL: Right. But it's more than that. These are people who psychologically like their job and are brilliant with materials, gadgets, if you like.

LIEBESKIND: I met the category in Madame [Denise Albe-] Fessard's lab [at the Institut Marey in Paris] when I did my postdoc there in the mid '60s [Madame Fessard (1916-2003) was the first IASP President 1975-78]. I've never seen that in the States.

WALL: Quite. Anybody that smart in the States is a company president, certainly with a PhD, and such things.

LIEBESKIND: Or thinks he ought to be. [they laugh]

WALL: So that I don't think it's a compliment to our society that such people existed, and by the way, I suspect that they are fading here for precisely the same reasons that they faded in the States. The States had some such people -- there was a man that you may know, Bernie Tursky.

LIEBESKIND: Yes.

WALL: He was our technician at MIT. Never got a university degree and absolutely brilliant, who became a professor at --

LIEBESKIND: Was it Pittsburgh?

WALL: No, I'm blocking...SUNY [State University of New York branch] on Long Island. [Tursky, who never earned an advanced degree, became a well-known psychophysicist and taught at Yale and Harvard as well as SUNY.]

LIEBESKIND: Stony Brook.

WALL: Stony Brook, yes. Now Bernie was revolutionary, politically [they laugh]. So I'm saying what I found here in Britain. I was adopted by and adopted some absolutely fabulous technicians who simply adored doing things.

LIEBESKIND: It really saves a lot of time and allows you to focus on the issues.

WALL: But it also allows you to be much more inventive in terms of technique.

LIEBESKIND: Quite so. All right, we've got you now all the way back in London, but of course, we've left out the gate [control model]. And your interaction with Ron and so forth.

WALL: Okay, so now let's start with that, with pain.

LIEBESKIND: With pain, because we really haven't talked about it or used that word yet.

WALL: Right. Except that, you see, I was looking at general properties of the nervous system, synaptic transmission and so on.

PATRICK WALL INTERVIEW

TAPE ONE, SIDE TWO

WALL: I was looking at synaptic transmission; I found it easy to record from single units in spinal cord, which not many people had done at the time. Some people in Sweden had done -- they really hadn't done it very seriously. And then so, obviously, instead of hammering away with electrical stimuli, I became interested in looking at natural stimulation. And I was simply astonished right from the first animals, because naively I'd simply accepted without thinking or questioning that of course I was going to find highly specific cells as predicted from a lot that was known at the time about peripheral nerves. A great deal was known about single peripheral nerve fibers in terms of stimuli and specificity and so on. So what I saw instantly was that these cells which were clearly receiving a massive convergence. And that was where it all began, because I then started looking for these specific cells. And so around about 1960 I published a paper on these cells that responded to brush, touch, pressure, temperature. [Cord cells responding to touch, damage, and temperature of skin. *Journal of Neurophysiology* 23 (1960): 197-210.]

LIEBESKIND: Is that the one on the brain?

WALL: No, this was an experimental paper. That was a more theoretical paper. And when I started looking for specific cells, I could on occasion find specific cells, but I could usually shift their specificity by mucking about with the excitability or something of that sort. So I knew I was instantly in a new frying pan from this previous one.

LIEBESKIND: Zotterman didn't call you into his office and tell you to shut up? [they laugh]

WALL: Quite. And this time, well, I'd had the previous experience and had a little bit more confidence of taking this line.

LIEBESKIND: A little older, a little tougher.

WALL: But also, don't forget, in that intellectual climate -- that was where people were of course looking at communication systems and of course didn't expect lines to be dedicated. Recognizing, though, that in another part of Boston there were people like [David H.] Hubel and [Torsten N.] Wiesel, who were in their way supporting the classical lines, with Lettvin very much in between, showing visual units extracting certain components of the input and selecting not just on the basis of the simple aspect of the input. [Hubel (b. 1926 in Canada) and Wiesel (b. 1924 in Sweden) shared the 1981 Nobel Prize [with Roger Sperry] for their work on information processing in the visual system.]

So it didn't seem completely wild, either from a general point of view that one would have multipurpose signaling cells, nor that you didn't have the mechanism to manipulate inputs and select certain patterns, time patterns, space patterns, and so on. Quite a lot was becoming known

about how that could be done. So at that stage, then I started thinking back to my clinical experience and did we really understand what you saw in the patients.

LIEBESKIND: You haven't said anything about that clinical experience. Are you talking now about pain per se?

WALL: Being brought up at that time in a classical medical way with an emphasis on neurology and an emphasis on symptoms as just being signposts, not something to be taken terribly seriously except as signposts that pointed at *the* diagnosis, with the whole thing being an intellectual crossword puzzle, in which you put all the signs and symptoms together in order to define what it is you should really be looking at. And then realizing that a lot of the pains which were simply accepted: "Well, you see that sort of pain in this sort of patient" -- weren't explained at all by assuming that all the problems had been solved in the periphery. So that was that.

At this time, with a completely different background or a fairly different background, there was Ron Melzack, with whom I've really never worked in my life, we'd only got to talking. He had worked with [William K.] Livingston [(1894-1966), surgeon and pioneering pain researcher at the University of Oregon] on some sort of classical neurophysiology, so that he knew about physiology. But what he really knew about, which was highly unusual, was animal behavior, which was clearly very odd indeed, if you wanted to have specific systems. So he and I got talking together. You ask about the gate control theory, which is 1965 as published -- if you read what we'd published certainly three years before [Melzack R and Wall PD. On the nature of cutaneous sensory mechanisms. *Brain* 85 (1962): 331-356]-- it says exactly the same thing in it. [they laugh] And we tossed a coin, and I published essentially exactly the same paper -- or, he and I did, only as Wall and Melzack rather than Melzack and Wall, and it was utterly ignored.

LIEBESKIND: What's in a title, eh?

WALL: Yeah. And then we put out the *Science* paper. [Pain mechanisms: A new theory. *Science* 150 (Nov 1965): 971-979.] And as you see, if you read this, we simply tried to bring together everything that we knew and what was in the literature at the time, knowing very well that we could be wrong, and certainly in the details.

[INTERRUPTION]

WALL: For example, at that time no clear-cut category of nociceptors in peripheral nerves was clearly discovered. They had been suggested but it was not clear that they were not just the end of a spectrum, but we said: "And if it turns out that nociceptors are a clear-cut class, it's not going to make any difference to what we're now going to talk about." So it wasn't that we were against nociceptors, it was how would you handle impulses generated by intense stimuli.

Now, there is a curious episode in this. Warren McCulloch had a huge farm in Connecticut to which one was permanently invited, and there were a whole gang of people who spent weekends on this farm, including me.

LIEBESKIND: Where was it?

WALL: In Connecticut.

LIEBESKIND: I'm from Connecticut, I'm just curious as to where.

WALL: Ah. Old Lyme, just off the shore [of Long Island Sound] by the entrance of the Connecticut River.

LIEBESKIND: Oh sure.

WALL: The McCullochs had built up the farm since the 1930s over quite a large area, in fact a whole little valley, which he dammed up and there was a large lake in it. Any rate, as happily part of being invited over the weekend, there was lots of work to do. I mowed a giant area with a machine mower and noticed that at the end of this my hands were numb. And I thought, that's very odd, why does vibration, really quite gentle, leave you numb? And so in fact the very first thing I did was to go back in the lab and have a look at what vibration did to these central cells. So -- I'm blocking on the name [John R. Cronly-Dillon, now Professor of Optometry and Neuroscience at the University of Manchester] -- we published this and called it "Pain, Itch and Vibration" [Wall PD and Cronly-Dillon JR. *Archives of Neurology* 2 (1960): 363-375].

LIEBESKIND: Right. Early '60s.

WALL: Yeah. So I already knew this odd business that these low-threshold inputs were interfering with the high-threshold inputs. So I then went back to the stuff we'd done in the mid-50s, this interaction between dorsal root volleys, and my whole attempt to unravel that, and saw that these large low-threshold afferents were generating one hell of a primary afferent depolarization, which was evidently preventing the action of the smaller fibers. So that's all in there. And bits of it were published. I think the real trick came, though, when I put that together and said, well if that's true, we ought to be able to drop pain by giving low-level stimuli. So I tried vibration. I knew that vibration inhibits, but it's a pretty crude business and so why not use electrical stimulation, which we tried in animals, where obviously you can produce just an input volley only in large afferent fibers. So then tried on myself and then went to [William H.] Sweet [(1910-2001), Professor of Neurosurgery at Harvard, Chief of Neurosurgery at Massachusetts General Hospital 1961-1977, and an early leader in the American Pain Society) and said, "Look at this, try it on yourselves, why don't we try it on some patients?"

LIEBESKIND: To Bill Sweet?

WALL: Right. So within --

LIEBESKIND: Did you know him already at this time?

WALL: Yeah.

LIEBESKIND: Bumped into him?

WALL: Right. By the way, much more important than that for me at that time and later was [Derek E.] Denny-Brown [(1901-1981, New Zealand-born neurologist and neurophysiologist], who was professor of neurology at Harvard, just fabulous -- never believed anything, absolutely my sort of bloke -- I never understood what he said, but it rang a bell.

LIEBESKIND: He was a great iconoclast?

WALL: Absolutely, yes, really great. So I must say, he was the one I had intellectual contact with. Sweet was around and a friendly, helpful bloke. So we then made surface electrodes and stimulated peripheral nerves, which of course thousands of people had done -- I mean, not for this purpose -- and then intentionally set about doing it to counteract pain. I really didn't know how to do that and we used relatively small electrodes which were actually quite difficult to maneuver.

LIEBESKIND: I don't understand -- why would they be difficult?

WALL: It turns out you need big electrodes, not small ones, but I was still sort of locked in with this idea of small.

LIEBESKIND: Smaller is better.

WALL: That's right. And of course, it in fact becomes quite hard to stimulate a deep nerve, particularly with small electrodes, because you get such high currents in the skin that it starts hurting under the electrode. So then I thought of my Yale days and why don't we stimulate the nerves themselves. So I went to see my friend Alex Mauro, who had had fifteen years' experience of buried electrodes. And he had a fellow technician turned company president called Avery [presumably the head of Avery Laboratories in Farmingdale, New York], and Avery promptly had made nice electrodes that you could fit around peripheral nerves.

LIEBESKIND: Cuffs of some sort?

WALL: [Silicone] Cuffs, and buried, and they had worked out all the technology, and buried radio frequency stimulators. So after Sweet and I had tried partly with surface electrodes and partly with putting needles up against a peripheral nerve, through the skin, we did some patients with these buried electrodes.

LIEBESKIND: This is patients still.

WALL: So then we moved to patients, both surface electrodes and cuff electrodes and for tests, stimulating needles brought up against the nerve.

LIEBESKIND: What I recall is a study with just volunteers with -- it must have obviously been surface electrodes, but these are now patients with, like, trigeminal neuralgia or something of this sort?

WALL: Well, peripheral nerve injuries in the arms, and then we tried things like diabetic neuropathy and so on. And then it seemed to me that we were going to -- the idea would be to stimulate a larger number of nerve fibers, and so we needed to go more centrally in order to get large numbers. In that same paper you will see that we put electrodes down hypodermic needles onto the spinal cord. [Wall PD and Sweet WH. Temporary abolition of pain in man. *Science* 155 (Jan 1967): 108-109.]

[INTERRUPTION]

WALL: I was just saying the last phase of this very rapid development -- cancer patients who were going to have phenol injected around their roots [to kill the nerve cells], said, hold on, when you've got a needle in, we'll stuff a stimulating wire down and stimulate their roots. So, just literally for ten minutes or half an hour, we stimulated roots of these patients in such a way that the paresthesias [skin numbness or tingling] overlaid the pain and sure enough they could get some drop of pain. So that was that, except that a resident of Sweet's at that time was Norman Shealy [C. Norman Shealy (b. 1932) now runs an alternative-medicine center in Missouri], who said, okay, well, we'll go a stage further and stimulate the dorsal columns, and so that's where the dorsal column stimulation came from. So I really do think that it was that that made people pay attention to the gate control theory.

LIEBESKIND: That there was a clinical utility.

WALL: People said that "We don't understand what the hell the theory is, but at least here's something that reduces pain, which wasn't obvious." Many people still can't understand how it works and think that you are blocking peripheral nerve fibers or stuff like that, that's been repeatedly shown not to be the case, or jamming, and they use all these analogies that don't apply to the nervous system. Okay, so I think that was one important pair of really almost accidental -- I wanted to do it on man to prove that the animal results applied, but it had an impact.

Now the other thing that was going on at that time was not for me to say, but for other people to say, but I really do think the entire atmosphere was changing. [Willem] Noordenbos had written his book [Noordenbos, a Dutch neurosurgeon, published his medical thesis, *Pain,* in 1959; it proved highly influential]. There was a general dissatisfaction with an understanding of pain and, much more important, a general dissatisfaction coming from people like Cicely Saunders of the treatment of pain. I mean, Bonica and so on -- an admission that people weren't coping with existing pain and, okay, it was a symptom and just to be dismissed and you really ought to be attacking the basic fundamental causes; but in the meantime, what are you going to do about these poor bastards in pain?

LIEBESKIND: Somehow there was something about gate theory or call it what you will, that was a little closer to the angels, wasn't it? I mean, to the clinical side of things? I mean, specificity somehow just didn't translate into the clinical picture at all.

WALL: Yes, but of course there certainly was not acceptance by the physiologists, who because -- I don't know if you have seen what was written at that time about this. The physiologists were

livid and open about this being clear impossible nonsense -- could not be the case, must be some sort of artifact. Even if they had bothered to read the experimental evidence, they would rubbish it. And so that meant that not only the old boys like Zotterman, Adrian, and Eccles, certainly, but my contemporaries like [Edward R.] Perl [b. 1926, Perl, now Kenan Professor of Cell and Molecular Physiology at the University of North Carolina, best known for his identification of and research on the nociceptive nerve fibers] and [Ainsley] Iggo [b. 1924 in New Zealand, Iggo, best known for his recordings from C-fibers in the 1950s, is Professor Emeritus of Veterinary Physiology at the University of Edinburgh and a past President of IASP (1981-84)] and Schmitt and so on, were antagonistic.

LIEBESKIND: Why were they so invested? I mean, why does anyone get so invested in an idea that, when new information comes along, they can't look at it uncritically? How do you see that?

WALL: Don't forget, they were committed to the hilt and had written absolutely clearly that this peripheral nerve fiber explained that sensation, and finish.

LIEBESKIND: Well, before we go more along the repercussions and the outcomes and consequences of the gate, let's go back a little bit more to the beginning of it. I mean, you just mentioned briefly that you and Ron had never actually worked together in the same lab, but you used to talk together.

WALL: Right.

LIEBESKIND: When did that start? That was at MIT?

WALL: Oh, surely 1960, at MIT.

LIEBESKIND: You became good friends at that time? You met him in some manner, and started chatting.

WALL: Oh yes. I met him because psychology at MIT at that time had been more sociology than anything else, really had no animal facilities, so poor old Ron, who had been appointed and was an experimentalist, had nothing to work on. So we, we being the biologists and electrical engineers and so on, being the kings of the time, were able to bring in these poor neighbors.

LIEBESKIND: Do you remember the first time you met Ron?

WALL: I think just exactly that -- a chap wandering around looking for somewhere to park a dog.

LIEBESKIND: Looking for work.

WALL: No, no, he knew the work and needed somewhere where he could raise puppies.

LIEBESKIND: These were like sensory deprivation experiments, those experiments from the good old days?

WALL: Yes, right.

LIEBESKIND: Did you become friends and start talking right away?

WALL: Sure, yes, because I certainly didn't know about his behavioral stuff. And I only vaguely knew about Livingston, Stotler and those people. [W. A. Stotler, a neuroanatomist, was the co-author, with Melzack and Livingston, of a well-known article, Effects of discrete brainstem lesions in cats on perception of noxious stimulation. *Journal of Neurophysiology* 21 (July 1958): 353-367.]

LIEBESKIND: So at that time still -- let's get to the word pain here now really -- would you say in 1960 you were interested in the subject of pain?

WALL: Oh absolutely, because I'd come across this total paradox in terms of mechanism, which was that the expected specific cells, I just couldn't find them. So that was a big trigger that was something seriously wrong here. Which then made one go back and back and back, partly to the patients and partly to the whole theory. [Psychologist Edwin G.] Boring [(1886-1968), at Harvard from1922] was still there, by the way, at Harvard at that time -- marvelous to talk to.

LIEBESKIND: I actually had a class with him.

WALL: So, but I suppose another more general background of something was very much in the air at the time. [Karl S.] Lashley [(1890-1958), American psychologist who studied learning as a function of the cerebral cortex] and [George E.] Coghill [(1872-1941) American neuroanatomist and physiologist, who worked at the Wistar Institute at the University of Pennsylvania], all of these people, were proposing that there was the alternative of a loosely wired nervous system from which you could crystallize moment to moment the working nervous system.

LIEBESKIND: Other than a hard-wired system, something that is made up of living connections and changing, plastic --

WALL: Exactly. Well, plasticity wasn't admitted at all at that time -- it was assumed that the entire nervous system on which you worked, i.e., spinal cord, brain stem, thalamus, was rigidly wired by the early neonatal stages, and that was it. And that the only variable connections were somewhere in memory systems that nobody was looking at yet.

LIEBESKIND: Well, now, of course Ron, via Don Hebb [Donald O. Hebb, 1904-1985, McGill psychologist, who argued for a complex, dynamic model of behavior] and [Austin H.] Riesen [(1913-1996, American psychologist and animal behaviorist, who held similar views] and so forth, that was all part of a tradition there, an intellectual tradition.

WALL: Exactly.

LIEBESKIND: The visual system, and pain, I guess, with the Scottie dogs. [Liebeskind refers to Melzack's famous early experiments with dogs raised in isolation, who had to learn to react to a painful stimulus]

WALL: Right.

LIEBESKIND: There was an idea that there was a more dynamic organization.

WALL: Quite. So I would say in every part of biology, there was this discussion, even in genetics, you know, there was a fight going on throughout on the role of genes as fixed structural determinants vs. modifiable things -- so that we were just one fraction of a very much more general argument going on, that we were very well aware of at the time.

LIEBESKIND: Let me ask you kind of a dumb question. I have long believed at some level -- I mean, I don't have any real evidence of this -- that there are personality types in science and that sort of who we are determines the way we are scientists and the kinds of concepts that appeal to us and so forth. And if you take gate theory v. specificity or whatever, or hard-wired v. more dynamic -- you can also get to a kind of concept of simple vs. complicated.

WALL: Right, right.

LIEBESKIND: Some people, wouldn't you say, just are not prepared to think of their science in complicated terms, they want it to be very simple. Is there some theme there? How would you…?

WALL: Absolutely. And I think, you know, it's expressed in these days that people are choosing between these sort of buzzwords of reductionist vs. synthetic, whereas the reductionist person really believes, Jim Watson fashion, that if you break down a structured system, no matter how complex, into its individual components, you are essentially there, you have solved the problem of how the whole thing works, that the sum isn't greater than the sum of the parts. And I quite agree with you that there is then a personality type that opts for this Swiss watch picture of no matter what system there is. It ticks away in a highly reliable fashion.

LIEBESKIND: You might even say a Swiss mentality, a cuckoo clock mentality.

WALL: Yeah. No, so I think these arguments go on -- as I say, it's fascinating to see genetics that looks now like the ultimate triumph of determinism -- there's a subculture of argumentative characters who talk about epigenetics [chemical changes to DNA which alter genetic expression, without changing the genome's structure] and so on, who know bloody well that there's more to it than this.

LIEBESKIND: So really these things happen in all domains of science.

WALL: Right.

LIEBESKIND: Probably not just biological science, but --

WALL: But I wouldn't say -- in physics, I really do think that reductionism does triumph, and one of the very reasons why physics is not biology and biology isn't physics is it really was determined, and I think the physicists were absolutely right -- eighteenth century, nineteenth century -- that if you found an electron, you didn't ask, why is it there, what is it? You were very, very satisfied to have found an electron, and then to be able to reverse the process and say, okay, we'll put two electrons together and see what happens. Now Watson -- if you take him as an example -- he says in the life sciences there are only atoms and molecules, and after that it's all social work. [James D. Watson, b. 1928, Nobel Laureate 1962 for his co-discovery of the structure of DNA.]

LIEBESKIND: So, that's that.

WALL: And it's the reigning theme, certainly of biology, and still the theme in the neurosciences.

LIEBESKIND: For every twisted thought, there's a twisted molecule.

WALL: Yeah. So that if you want to attract attention with a paper, you say that stimulating the amygdala produces instant death. Nobody is particularly interested unless you add "by way of peptide upregulation." [they laugh]

LIEBESKIND: Right, right. You know, I think I want to go back to the gate again. I want to get back more to the origins of it and some of the dynamics maybe that went on with you and Ron. You had done the empirical work, you understood the dorsal horn at that time and the inputs and the changes and so forth. Ron was coming from a very different tradition of animal behavior.

WALL: Plus his experience with Livingston on pain patients. He'd already begun collecting what amputees said about their pain and he'd been collecting a vocabulary and seeing that people were talking about very different things.

LIEBESKIND: For the sake of history -- I mean, people are going to want to know more about -- I want to know more about -- What went on in those early conversations between you? Did you just sit down and kind of write the damn thing? Did you write a draft and he wrote a draft?

WALL: Frankly, I don't believe it was very interesting. I am sorry to say that this was no intellectual triumph, because we were both so much on the same side and in a clear minority. Our worries were what those buggers are going to do, not to argue out between ourselves about these things. And in a sense we did have a division of labor -- I thought and still think in terms of relatively limited neuronal circuits. He thinks about whole animals and people.

Now, I mean, going back to the personality business -- personality's maybe too pretentious a word, but I do think that there are acceptors and revolutionaries in the world, and I think probably Ron and I are in a group of people who are superbly dissatisfied, unbelieving.

Iconoclast doesn't mean that you are actually -- iconoclast means actually smashing the icons. I think, in our case at that time, the question was which icon to pick up rather than which one to smash. But, yes, I think that -- you know, there's an interesting subdivision -- somebody said the world is divided into two types of people -- one of whom say the world is divided into two types of people! [they laugh] But I think there are two types of academics, and whole cultures, where the nicest thing that you could possibly do is to show that your teacher is right, vs. the best thing you could do in academe is to show that he's wrong. Most people are in the first --

LIEBESKIND: It's almost a [Karl] Popper [(1902-1994), Austrian-born British philosopher of science] sort of philosophy of science idea vs. that science only moves forward by showing things that are incorrect, moving on from there. Or what [B. F.] Skinner [(1904-1990), American behavioral psychologist who traced all behavior to operant conditioning] said once, that if an experiment works out the way he anticipated, he feels disappointed because he hasn't learned anything.

WALL: Right. I do think in a general way that there is then a culture of questioning, groups of people who feel more comfortable questioning, and groups of people who feel exceedingly uncomfortable with questioning what is going on. I have to say here an aside. Because of the war and because of the school that I went to, my best friends have always been Jews. And, as it rapidly developed, left-wing Jews.

LIEBESKIND: Which in many people's minds is almost synonymous.

WALL: But isn't, unfortunately.

LIEBESKIND: But it isn't, not today.

WALL: I do feel, as you know, I've had a lot of experience which we may come on to, in Israel, that there was a historical slot of that type of Jew that I am talking about, but I am not certain that they are making them like that anymore. [they laugh]

LIEBESKIND: Starting from the top, Freud and Marx.

WALL: While I think that there was a time when I would positively explore somebody who seemed to me to be probably Jewish, thinking that I would probably have a good conversation, no matter what it was about, I don't believe I find that any longer with the younger, with the generation below me, and I think that happened some time ago, so that in one's cultural background, it so happened that I was lucky enough to be in the place and time of a bunch of very dissatisfied and verbal Jews. [they laugh]

LIEBESKIND: Some of these were, I mean, were these all in the United States, or this was when you were growing up in England?

WALL: Oh no, because growing up in England, as I said, at the time and the place, even immediately before the war -- very large numbers of Jewish refugees here and because of the

school happening to have a liberal tradition and taking on quite large numbers of those refugees, so probably half my classmates were in fact German Jewish refugee children.

LIEBESKIND: In the school? Before Oxford?

WALL: Yeah.

LIEBESKIND: Well, I guess there is a whole intellectual tradition in that socioeconomic group and religious group and so forth of iconoclasm.

WALL: Right. Not that many of them were religious. But they had a tradition of socialist, liberal, dissatisfaction with given answers -- I think that was in there certainly with Melzack and certainly with me. Much tougher these days, I think.

LIEBESKIND: There's a general conservatism, isn't there?

WALL: Yeah.

LIEBESKIND: You wonder whether it isn't the poverty -- well, it's not really the poverty always, I guess, but the difficulties that don't breed this -- the difficulty in life makes you more questioning. I guess this wasn't your own circumstance, presumably, but --

WALL: And I'm not even certain -- I once talked with Sidney Brenner -- Sidney Brenner, a student of Crick's and really the developer of cloning and of all sorts of things; (Brenner, b. 1927 in South Africa, now at the Molecular Sciences Institute, in Berkeley, California, received the Nobel for his work on the genetic regulation of organ development.] And I'm blocking on the name of another Nobel Prize winner at Cambridge (Aaron Klug, b. 1926 in Lithuania, but raised in South Africa, Nobel Laureate in Chemistry 1982) -- they talked about a tiny group from Johannesburg, of South Africans, who had done fantastically well, and they described their background, '20s and '30s, of -- maybe their parents had suffered or their grandparents had suffered -- actually *they* were in clover. They were in a very settled, opulent environment that somehow produced an astonishing number of these questioning, really non-neurotic types, and certainly not suffering -- no artists in garrets business. And I think that --

LIEBESKIND: It's a generation or two from that, isn't it? Hard to know where these things come from.

WALL: Or how to produce such a society.

LIEBESKIND: So you and Ron hit it off from that standpoint, obviously.

WALL: Sure, yes.

LIEBESKIND: Okay. Let's talk more about the aftermath.

WALL: Okay, so I think we should go on to after that. So there was -- This now includes me coming back here, which I don't think was terribly relevant in terms of the intellectual development, because the work just continued very nicely and spun off into various other directions, like realizing that the more intact the animal, and the freer you could observe, the better, so that I went into recording from freely moving animals, which immediately I found the results so complicated that I just couldn't cope with them. I could do it technically, but I didn't know what the animal was doing.

LIEBESKIND: Right, couldn't control.

WALL: That's right. But from that came coming here to London and thinking maybe the dorsal column nuclei would be simpler than the spinal cord, which I don't think they are. And then, for example, John O'Keefe started working with me, and his whole hippocampal story starting from that – [O'Keefe is still working on the hippocampus as a group leader at the UCL Institute of Cognitive Neuroscience.]

PATRICK WALL INTERVIEW

TAPE TWO, SIDE ONE

WALL: So the developments of details, and now just talking about the science and me. At the time of the gate control theory, I was actually still thinking in very conservative terms. The only changes that I imagined could occur in the nervous system were using the classical, well-discovered, Sherringtonian changes, produced by summation, inhibition, and facilitation and whatnot. And I imagined that the nervous system really was all working that way. And that, if anything, really the basis at the time suggested that was perfectly okay. If you understood a single jerk of a muscle, then you also understood tonic contraction of a muscle; it was just the same thing repeated as long as you please, there really wasn't any need to go further. Long-term events were just repetitions of short-term events. Finish.

And now going back to H.T. Chang, H.T. Chang had shown me a very remarkable experiment, and that was (at the time it was a very popular thing) reverberating circuits, which was by the way another explanation for long-acting things, you just ran nerve impulses around in circles.

LIEBESKIND: Started something going.

WALL: And a popular reverberating circuit was one that Eccles and Anderson had shown. They'd recorded in thalamus, sent in a volley and saw -brm- the cells respond, and then -brm brm brm- respond somewhat more. And they said, ah, this is because the impulse is going up to the cortex, back down to thalamus, back up to cortex and so on. And the evidence was you lop off the cortex, send in the volley and it just goes -brm. Fine. And that is still the standard example of the reverberating circuit. Chang had said, "Let's give this time. There's something called shock or diathesis [reaction to stress]; maybe the system is shocked by removing the cortex. Why don't we let it settle down for a bit, a few hours, in this case?" And lo and behold, the reverberations return without cortex, evidently not depending on thalamocortical circuits.

In 1970, I decided to start marching into the head. I was already trying with these long-term chronic recording electrodes, and David Egger [now Professor of Neuroscience and Cell Biology at Rutgers University in New Jersey] came to work with me, and we were going to do a very simple experiment which had in fact been done before -- Perl, I think, had done it. We were going to record in thalamus, send in an afferent volley, and ask the question, how much was going up the dorsal columns and how much was going up other pathways. And we knew that both were somehow getting there and we wanted to know what's the relative importance of one vs. the other. So we mapped thalamus, took out nucleus gracilis, which happens to be very easy to do in a rat, and saw a hole in the map of the body. Thinking back to old Chang, I said, let's wait a bit, and in fact we waited some days.

LIEBESKIND: After the lesion.

WALL: Yes. And to my astonishment, this hole had almost completely filled in with the nearest intact afferents. You know, I was really amazed. So that set me off on looking for longer-term

changes. Thalamus seemed to me, and cortex, which had also shown us this was happening, seemed to me, to be hopelessly complicated, and no place to analyze. So I went back to the spinal cord.

LIEBESKIND: Leave that to the social workers! [they laugh]

WALL: That's right. Went back to the spinal cord, which I knew how to cope with technically and also seemed to me to have the advantages that I had an input under control and an output under control and so on. Now, somewhat related to this is that one of the people who did with me the last classical spinal cord experiments in which we were defining precisely single receptive fields -- what the components were which went to make up a single receptive field -- was Peter Hillman, a most astonishing fellow, have you ever met him?

LIEBESKIND: Never. I know his name.

WALL: Amazing character. South African in origin -- because of an accident of the war, was marooned in the United States as a teenager in the war with his mother, the accident being they happened to be visiting the States, traffic across the Atlantic was closed down, and they stayed in the States. And he as a guaranteed disgraceful genius had managed to get himself a PhD from Harvard in physics at the age of 19 or something obscene like that. [they laugh] And had gone around and had gradually worked his way up in the physics world, so that by the end of the '60s was head of physics at the Weizmann Institute [of Science] in [Rehovot] Israel. And had decided that the life sciences were much more interesting than physics, and turned in his chairmanship and professorship, spent a year just reading, and then spent two years as a sort of aged apprentice, one year with me and one year with [Haldan K.] Hartline [(1903-1983, Nobel Laureate for his work on the physiology of vision] at the Rockefeller on Limulus [*Limulus polyphemus*, the horseshoe crab].

LIEBESKIND: You were in London at this time?

WALL: Yes. And in fact he, for reasonable reasons -- light on invertebrate photoreceptors was a little bit closer to his background than the horrible sight of lamina five cells sloshing about from one state to another -- went and in fact started his second of his three careers and is a professor of neurobiology at Hebrew University with a good reputation in invertebrate photoreceptors [today Hillman is Professor Emeritus at the Silberman Institute of Life Sciences]. His third career, which he's recently started, is that he has set up a museum for -- an exploratorium, a museum where you have to be active, which is spectacular, in Jerusalem.

LIEBESKIND: Incredible. It's an amazing thing, just to give up a chairmanship, a professorship, and just go over to something completely different.

WALL: Quite. In a sense, one of those Jews I've just been talking about. And again, coming from a comfortable, well-to-do background, I'm sure his parents or perhaps grandparents had had tough times with Cossacks and whatnot, but certainly he hadn't.

LIEBESKIND: Was this the beginning of your Israeli connection, by the way?

WALL: Right. So he in 1970 had invited me to Israel, and there I met Vera, whom you met, and we eventually married. There were all sorts of reasons for me then to be commuting between here and Israel, and I set up another lab in Israel. By this time, with this appearance of plasticity, which was to turn out to be highly relevant, I again did a classical way of thinking by saying, "Well, let's start in the periphery." You know, Adrian had said that all central phenomena can be observed in peripheral nerves, which is probably true.

LIEBESKIND: It's a challenging statement, anyway, worth taking a look at.

WALL: Right. Any rate, so thinking about plasticity and then asking myself and now really going back to this pain problem, and now with the question of the peripheral nerves and having treated quite -- by this time quite a lot of people with damaged peripheral nerves, I said, well, we'd better have a look at damaged peripheral nerves. Which had been done astonishingly little. Really almost no literature at all, which I adore to take up a subject with no literature in it. And it was just assumed that you cut an axon and it seals over and becomes just like it used to be.

LIEBESKIND: That's another dimension, isn't it, by the way? We spoke about the iconoclastic thing -- but it's another dimension, I think, of this is is the interest in going into uncharted waters.

WALL: Oh yes.

LIEBESKIND: I mean, isn't that another characteristic of Patrick D. Wall?

WALL: You know, one of my heroes is C. Judson Herrick[(1866-1960), American neuroanatomist], who said, "To be successful in science, you need to do three things. One is to find something nobody else is working on, two, write a book about it, and three, start a journal." So he in 1905 was looking at the brain of the tiger salamander, which was revolutionary in its day. Why bother with a silly invertebrate when you've got a man you could look at? And so he wrote *The Brain of the Tiger Salamander* (1948) -- by the way, very much in that tradition, this Coghill tradition, is this thing a diffuse network originally which crystallizes out and so on? And he started the *Journal of Comparative Neurology*.

Yes, so I think there are very, very practical reasons for starting on something nobody else is working on. It clearly requires a certain -- it's not really guts, it requires a certain confidence, because you might starve to death, and one just has to have the confidence that you're not going to starve to death. I mean, why peasants are not revolutionary characters is because it's bloody dangerous to start mucking about. The safest thing to do is to do exactly what your father and grandfather did -- at least they survived.

LIEBESKIND: And the academic analogy holds. A lot of people just follow what their academic parent did.

WALL: Right. And, I mean, translated also into grant origins, that the committee is going to be of a group of people working on popular subjects -- that's why they're there. You go along with some unheard-of subject, they're likely to find reasons for not funding you.

LIEBESKIND: Until this last time, the only time I ever had any grant trouble was when I proposed something really quite different.

WALL: Quite.

LIEBESKIND: Which we were working on and we knew we could work on it, but they said, no, no that's not -- they knew who I was, and they said, go back and do this because --

WALL: It's your thing.

LIEBESKIND: That's what you do. We went ahead and did it anyway.

WALL: So, I mean, it's true that it obviously becomes progressively more and more difficult to find a new topic, but it's also clear that -- and that there are apparent rewards for doing something in the popular accepted ones.

LIEBESKIND: Maybe it's too early in the interview to ask this question, but it seems to me, this observation -- it seems to me that plasticity really is a concept that goes throughout your career, does it not?

WALL: Yeah, but as I said, it shifted, the plasticity -- in the '60s, I imagined that we had all the – [that] classical physiology gave you all the possibilities for all the plasticity you needed.

LIEBESKIND: Now you're talking about the mechanisms of plasticity when you say that, are you not?

WALL: True.

LIEBESKIND: But the fact that there can be change, and that it's not just hard-wired.

WALL: Oh, absolutely, right.

LIEBESKIND: Maybe there's something psychodynamic there -- we won't bother with that. That's the river I see there, huh?

WALL: Oh yes, if it weren't for those bloody trees -- in the winter there's a magnificent view from this window. In fact, you don't need a watch -- Big Ben is behind those trees. So maybe we can come back to that. So I started then looking at peripheral nerves, and this was strictly because of being suspicious about what the patients were doing with peripheral nerve lesions.

LIEBESKIND: With peripheral nerve damage. By the way, may I ask, to what extent does your clinical training come in? I mean, it seems to me more recently we have seen more of that from you, when you see patients or you make observations.

WALL: I always did, all along.

LIEBESKIND: All along -- you and Noordenbos and that remarkable person with the knife in the back.

WALL: Oh yes. [they laugh]

LIEBESKIND: The doctor in you keeps, the physician keeps coming to the fore.

WALL: You know, Warren McCulloch was once talking with the head psychiatrist here in Britain -- McCulloch was professor of psychiatry at Illinois, and this chap said to him, how long were you a practicing psychiatrist, and McCulloch said, six months. And this man drew in his breath and said, "And do you think that six months in psychiatry gives you the right to be called a professor of psychiatry?" And McCulloch said, "I think anybody with half a brain in his head would see enough problems in six weeks to keep him going for the rest of his life without --" Which I think is correct. [they laugh]

LIEBESKIND: Defining in terms of the question rather than the answer.

WALL: That's right. But that doesn't mean to say that as you think about it, that one shouldn't go back to the patients, because they'll ask you new questions or demand that you find the answer to new questions. So yes, I don't think that the questions come out of the laboratory. I think answers may on rare occasions, as you say, about the nature of mechanisms and so on. But the phenomena to be explained, those are clinical things, and by that I don't mean human psychophysics. I think the trained subject is an example of a domesticated animal who is being taught to restrict his repertoire to something unbelievably silly and artificial.

LIEBESKIND: Like some *Felix domesticus*.

WALL: And cats are much smarter than that. So that to do pain experiments on human volunteers, where the start point persuades the subject that they're not going to be damaged, and that instantly puts this person into a very peculiar category.

LIEBESKIND: But you know, again, I think the pain field is not necessarily unique, but it must be at least unusual in this bringing together of clinical and basic science folks, and that's something I think we can ascribe at least partly to the development of the IASP and the related organizations that bring clinicians and basic scientists together. It seems now that the pain field, as I just read the table of contents of the journal *Pain* for the last few years, here are all these basic scientists with no clinical training, doing research on peripheral nerve disorders and so forth, on pain of neuropathic origin really, and trying to make the clinical connection.

WALL: Right. I still wish they'd go and have a look at a patient. Even without, I mean on the McCulloch line, that I don't think you have to have seven years in medical school to see that somebody with a causalgia is a pretty odd sight.

LIEBESKIND: To what extent have you seen patients over the years, and to what extent has that benefited your career? Do you ever do anything of a pain management or clinical --

WALL: I always made the rule that I would never ever take responsibility for a patient, so I'd always seen somebody else's patients.

LIEBESKIND: You're a consultant, you're an observer.

WALL: Yeah. But always then so that I wasn't just kibitzing or slumming or something, but that I really had a quite specific question -- I don't mean necessarily an experimental question. What does a patient say after a dose of morphine? What do they look like? And so on. Not me giving the morphine, not me making the diagnosis, because there are plenty of skilled physicians around. If I'm going to pour morphine on an isolated spinal cord, which may be perfectly justified, I better also be aware of what happens when a whole person becomes analgesic -- what else are they saying? and so on.

I think now it is true that having a medical degree gives you a union card and again a certain amount of personal confidence that you don't mind going up and poking a few fingers into a patient. But I'm, I think, saying it again and again that really going and sitting and talking, and you've got that rare luxury which most doctors don't have, of sitting and talking with a patient --

LIEBESKIND: Not having to generate your income by the volume of the patients you talk to.

WALL: Yes, quite. So that you talk about being with Noordenbos -- Noordenbos was a quite extraordinary person -- I mean, for starters, a neurosurgeon who hated to operate. He would operate under clear conditions where the chances of improvement were very high. He wasn't going to operate because somebody said this ought to work. But a sensory examination of a patient with Noordenbos was a good two days' work.

LIEBESKIND: Where did you first meet him, be influenced by him? You knew his book, of course.

WALL: You know, I'm very embarrassed that I didn't read his book for probably five years after it was out, and it was Melzack who stumbled across it and said, "Boy, look at this guy."

LIEBESKIND: When did you meet Noordenbos first?

WALL: I suppose about 1970.

LIEBESKIND: You and he were really very close, were you not?

WALL: Yes. About 1970.

LIEBESKIND: Was it in connection with IASP and the journal?

WALL: Probably.

LIEBESKIND: Oh no, not if it was 1970.

WALL: But you see, he was certainly in there at the beginning of IASP; and I'm not certain if he was at the Seattle meeting, but certainly he and I went to Elsevier, which was actually before the Seattle meeting that we had done this. I have to confess to you that I was very strongly in favor of IASP because I thought there ought to be a journal, *Pain*, and I didn't think there was enough interest in pain to float by itself and that there really ought to be a society, which for me in a totally selfish way --

LIEBESKIND: It would force its members to keep the journal economically viable.

WALL: Exactly. So it's not very complimentary to IASP, but I thought that was its function, as far as I was concerned.

LIEBESKIND: While we're on that topic, what was your first connection with IASP? Obviously, I remember you were at the Issaquah meeting.

WALL: Right. And pushing Bonica: "Let's form a society."

LIEBESKIND: So this was in the planning stages of that. Did you know Bonica -- that he was talking about this, or did he just call you or write you and say, we're going to have a meeting in Issaquah?

WALL: I've really forgotten. I don't remember. But certainly I went to Issaquah determined, pushing for a society with this hidden agenda, as I've said. By that time I'd reckoned that there really ought to be a journal. Because by that time, you know, a lot of things were brewing.

LIEBESKIND: Had you and he already discussed the fact that there should be a journal and that you might be its editor?

WALL: Again, I should know this thing. I've forgotten, but I certainly put it to him at that time.

LIEBESKIND: Had you ever met him before Issaquah?

WALL: I don't think so. [*Ed:* Actually Bonica attended and gave a talk at a course organized by Wall in Israel in April 1973, the Bat-Sheva Seminar, so clearly they knew each other prior to the Issaquah meeting.] I knew his book, which was another important thing -- also probably ten years after he had written it in that case, in the '60s -- I'd seen it [*The Management of Pain*, first published in 1953].

LIEBESKIND: What are your recollections of the Issaquah meeting?

WALL: Quite tense, because I wanted to brew this up into something, and, as I said, I was really focused on the need for a journal.

LIEBESKIND: Why? What was the need? It wasn't clearly just so that you could be the editor of it and have something to do -- it was that you felt --

WALL: No, the need which I'd already seen, that there were questioning people, anesthetists in particular, a few, very few neurologists, who were beginning to be thoroughly dissatisfied, not knowing what they were dealing with, seeing that they needed to redescribe the classical syndromes, for one thing, plus the neurophysiologists and pharmacologists.

LIEBESKIND: So in all of this heat that the gate theory generated from '65 to '73, in that eight-year period --

WALL: Right, plus all the central things that you know better than I, the whole PAG [periaqueductal gray area of the brain, where stimulation-produced analgesia can be demonstrated] business – Allan Basbaum [now Professor and Chair of Anatomy at the University of California San Francisco] was already with us, O'Keefe had found that these descending effects disappear if you cut the DLF [dorsal lateral funiculus] and -- so it seemed to me that there was a real subject brewing with a lot of people interested, certainly clinicians and certainly basic scientists, and by that time Bonica had come to the same conclusion, just in Seattle, let alone anywhere else.

LIEBESKIND: Yeah, he did. The way he tells the story -- I've talked to him about this -- is that much earlier he had discussed this with Livingston when he first was out on the west coast with Livingston. And Livingston said, "Oh, there are not enough people." And there probably weren't at that time.

WALL: That's right. In spite of the fact that, you see, Livingston had recruited Melzack.

LIEBESKIND: This may have been earlier, I don't know.

WALL: Oh yes.

LIEBESKIND: When Bonica first spoke to Livingston about it, he was discouraged. It may have been even before Ron went to work with Livingston.

WALL: Right. Because -- I've forgotten the dates -- mid-50s.

LIEBESKIND: Yeah -- I think of Melzack, Stotler and Livingston, that came out in '58, so a few years before that.

WALL: That's right.

LIEBESKIND: Did you have a sense then that creating a society and having a journal would itself promote the development of the field, not only that it is a receptacle for those who are in the field, but that it will itself be generative? It seems to me that's a very important concept?

WALL: Oh, absolutely. And of course, I was thinking in pretty academic terms, not in terms of what has happened clinically. And in fact it had certainly had been in my mind at that time and is still in some people's mind, the question about a separation of pain as a proper separate subject. I mean, my ideal of pain academically would be to reintegrate pain into a general sensory system, and similarly, I am not utterly convinced about a pain clinic, except as a demonstration that physicians in general aren't coping right, correctly. If they were capable of coping, then really departments of medicine and neurology and rheumatology and whatnot, the classical departments, ought to have been able to cope, and it was necessary to hit them over the head that they weren't coping, by having a separate discipline, a clinical discipline.

LIEBESKIND: Disciplines are walls, and, I mean, that's part of the problem.

WALL: Sure.

LIEBESKIND: That's why it's been such an advantage in the field of pain, breaking that down, having people talk and so forth.

WALL: Yes, and let's --

LIEBESKIND: I mean obviously, in terms of your own intellectual development, as you have recounted it here this afternoon -- you've been influenced by people from all different kinds of fields, medicine and from electrical engineering and psychology, I mean, the whole map.

WALL: Sure. But let's face it -- to be honest about members of IASP, in 1993, the majority of them are probably maybe dissatisfied with their own discipline and would like to form another separate walled-in discipline, called pain or whatever.

LIEBESKIND: Algology, or something?

WALL: One can see that in the various rivals to IASP, which are precisely what they set up, and there's a large fraction within IASP of exactly the same type.

LIEBESKIND: An inexorable tendency for people to build walls and say, well, we're a group.

WALL: Well, I don't know, I mean, partly, let's face it, it's good business. To hell with the bloody academics, it's another way of making money. I'm not being cynical, it's just a fact. And we know that there are -- there's been a struggle within the journal *Pain* about the balance of the content -- with people saying, we don't read this rubbish, why don't you tell us how to treat this, that and the other? This has been one of the great advantages of many of the other journals appearing, because that's just what they did, which then relieved the pressure on the journal *Pain*.

LIEBESKIND: Took some of the heat off.

WALL: And there were similarly pressures, for example, clinical psychologists concerned with pain really did not have any opening to publish what they were interested in, whereas a neurosurgeon or a pharmacologist had plenty of other places where he could publish. So that there was a period when it is perfectly true, there was a great deal of clinical psychology -- I don't know how good, but a lot of it -- in the journal *Pain*, which I was happy to see there without apology, because they had nowhere else to try to develop their subject. Now they've been sufficiently successful that actually they do have other places. I mean, even other clinical psychologists now admit that this is a topic, a permitted topic.

LIEBESKIND: You know, just to say, in these oral histories that I'm doing -- these are the kind of ideas too that I think are very important, and the concepts that have moved the field and so forth -- the idea that a journal can really itself be terribly influential on the development and the growth of the field. Oh, I believe that firmly -- you surely do. Why do you shake your head? Don't you feel that the journal *Pain* under your long stewardship has itself --

WALL: Well, obviously I would like to think so. I don't have a scrap of evidence that it all wouldn't have happened had this been distributed amongst a number of other journals and so on.

LIEBESKIND: I don't know how one could gather evidence on it, but it seems so evident to me that it is so. And that pulling it together and having this be the repository of the finest work that's going on in the field.

WALL: I mean, if you look at a number of the key journals and if I were to pick out the most important papers of the last fifteen years related to pain, sure, I'd like to say, yes, they appeared first in *Pain*. I'm not certain that I could defend that. First papers very often appeared elsewhere and then as it became elaborated, they said, okay, let's try *Pain*. I'm not running the journal down, but there's been certainly a continuous struggle that people may say, well, I'd like this to appear where physiologists would read it or where neurologists would read it.

LIEBESKIND: In their own disciplinary journal first.

WALL: Right. So I mean, while I would like to think you're right, that it's played a part in developing the subject of pain, I think it was the general intellectual development which really has snowballed, that this was a fascinating basic issue to do with sensation, to do with neurophysiology, and to do with clinical problems.

LIEBESKIND: Well, certainly you'd agree that having a journal of excellence in the field of pain, which the journal *Pain* has been, has lent great prestige to our field and helped to legitimize it in the eyes of others -- helped to form it as an entity.

WALL: True, yes. I think probably more in the clinical world, you know. On the grounds that there were prestige journals of physiology or whatever you like,
where still people might say, wow, I got that into *Nature* or *Journal of Neurophysiology* or whatever, therefore it must be good.

LIEBESKIND: All right, let's see where we are. I think the discussion so far has sort of touched on most of the questions I have. We sort of cut across a lot of things.

WALL: Yes -- I'd like to push forwards with this plasticity topic, because I'd really only just started with having lurched first towards investigating peripheral nerves. And I really do think I invented a subject which was the pathophysiology of peripheral nerves, which is still going strong.

[INTERRUPTION]

LIEBESKIND: This was the work with [Marshall] Devor in Israel [Devor is now Professor of Biology at the Institute of Life Sciences at Hebrew University in Jerusalem]?

WALL: Right. Then, with Basbaum and [Tony] Yaksh and Devor, first sticking to the CNS, where I'd been with Egger and cutting dorsal roots with Basbaum and then going with Devor and cutting peripheral nerves, and still seeing central changes -- that was an exciting, interesting time. [Basbaum worked with Wall at UCL in 1971-72.; Yaksh is now Research Professor of Anesthesiology at the University of California San Diego.]

[TELEPHONE INTERRUPTION]

WALL: Now the problem with what we had found in peripheral nerve was that these quite slow changes were taking many days to occur centrally. They might be morphological changes, sprouting changes. And that haunted the subject for a long time -- still does to a certain extent.

[INTERRUPTION]

WALL: So, how to get around the problem of morphology versus physiology -- so that took up the '70s for me. And then the '80s were how to avoid the discussion of these very long-term changes -- couldn't we find some quicker changes. So that then led me to, with Clifford Woolf, to the business of brief inputs producing within seconds or minutes things that lasted hours. [Woolf, born in South Africa, today holds the Kitz Chair of Anesthesia Research at Harvard and head the Neural Plasticity Research Group at the Massachusetts General Hospital.]

LIEBESKIND: Which is what's dominating the field now as a subject matter totally.

WALL: Right. So that plasticity worked then for me in going in these three stages -- one, seeing changes all to do with classical action potentials and post-synaptic potentials. Then seeing very long-term changes, which lasted forever, which looked like chemical transport, [and] may be morphological changes.

LIEBESKIND: That's the peripheral nerve work.

WALL: Right. And then being able to fill in the middle with changes that were clearly to do with nerve impulses --

LIEBESKIND: With the dorsal horn.

WALL: -- and lasted hours and clearly couldn't be morphological. Just to finish, I'm now into a new phase.

LIEBESKIND: Oh, okay. So we've gotten the Wall of the '60s, the '70s, the '80s, now we're going to hear about the '90s.

WALL: The '90s.

LIEBESKIND: Is it still under the rubric of plasticity?

WALL: Yes. And it's a completely new degree of freedom, although like all things new, of course, it has a background. Fortunately, again, in terms of the literature, very little background. And briefly it's the following: We had all accepted that if an action potential was started in an axon, it would get to the end, and at the end you could modify how much transmitter was released and so on. True. But it turns out that the transmission down the axon is under control.

LIEBESKIND: Oh really.

WALL: Now, that is not news at all -- the invertebrate people knew that all along, that how a silly lobster or insect copes with that horrible mass of neuropil [a dense network of interwoven cytoplasmic processes of nerve cells (dendrites and axons) and of neuroglial cells in the gray matter of the central nervous system] is they are shunting action potentials at Y junctions or T junctions -- they decide which one is active -- the whole thing doesn't go active unless the thing's been poisoned.

LIEBESKIND: Is it collaterals, axon collaterals you're speaking of?

WALL: Right. So the invertebrate people knew that all along. That said to me, "Well, if those stupid invertebrates learned that trick --"

LIEBESKIND: Why would we throw it away?

WALL: Quite. And in another way it isn't news, because that was partly the very thing that we had suggested in the '50s, was that presynaptic inhibition was actually a block of transmission to the terminals, not mucking about with the terminals, and we had some evidence. Any rate --

LIEBESKIND: So you're saying that at the Y junction there's now the possibility for it to go in one direction and not the other?

WALL: Right. Or, more subtly than that, and the thing -- I had been bugged by a paradox -- paradoxes start off everything. The following very simple paradox, known in the nineteenth century: A single axon comes into the spinal cord, makes a T junction, and one arm goes towards the head and one arm towards the tail. The one going to the head, okay, that can go on

forever, that's got to feed the dorsal column nuclei and so on. What's that branch doing going down towards the tail? Well, people said, you know, of course, it's not plugged in very exactly -- there's an area where things come in, and you've got a segment and so on -- so it needs a bit of space.

It's become apparent, and I'd known this now for a long time, that the axon going down towards the tail goes on and on and on. And they end in ludicrous locations; this is not just my work, other people have seen this. If you look at nerve fibers coming into upper cervical segments and follow them, as Granit had done with the greatest of ease with tracers, you find them still running in lower thoracic segments.

PATRICK WALL INTERVIEW

TAPE TWO, SIDE TWO

WALL The paradox is the following: You find primary afferent fibers running along in the dorsal columns, the descending branch. It's very easy to record from the post-synaptic cells, and if there are primary afferents there with perfect terminals on post-synaptic cells, why don't you see the cells respond? Which they certainly don't. Otherwise you wouldn't have a map in the spinal cord, if these things were splashing all over the place. So that had bugged me for some time. And I'm now just writing now paper five of a series; two are out, one's in press, and two about to be. So now you see, I've learnt one thing from all these years of struggling -- if you want to say something new, boy, you've got to get some real power up on the start line and clobber them all at once with it. Well, these things, two of them have been out and people are saying, well, that's pretty weird, isn't it. [*Ed:* The first three of these papers appeared in series "Long-range afferents in rat spinal cord") in *Philosophical Transactions of the Royal Society of London, Section B Biological Sciences* v. 334 (Oct 1991), 337 (Sept 1992), and 343 (Jan 1994).]

LIEBESKIND: Five papers! [they laugh]

WALL: So. Very simple. You know these axons are present, so you ought to be able to record action potentials in them -- you can't. You say, well, you know you can't report a negative finding like that -- you can't see an action potential, that's a big deal. So you've got to find a way in which you can make them conduct. So the first thing I tried, going back to all of these things -- how about cutting all the dorsal roots except the one that you're interested in? They conduct beautifully. They take quite a long time to do so -- days before they start conducting. So then I felt, well, what the hell is cutting the dorsal roots doing? Maybe the dorsal roots are controlling the membrane potential of the fibers. Is there any other way that we can muck about with the membrane potential of the fibers? And the answer is yes, the GABA system is in there; if you eliminate the GABA system, they respond spectacularly and so do the post-synaptic cells.

LIEBESKIND: So they are held under check by --

WALL: Right.

LIEBESKIND: This is GABA intrinsic to the cord?

WALL: Right. So that's nice and a nice example of a subject that somebody else is working on. What it's giving is another degree of freedom for delivering a plasticity -- you've got the classical EPSPs [excitatory post-synaptic potentials] and IPSPs [inhibitory post-synaptic potentials], you've got growth possibilities, you've got long-term potentiators, neurotrophic agents, and now a system deciding how far an action potential penetrates a terminal arborization. So that's it, that's where we are in August '93.

LIEBESKIND: Pat, how old are you? You're in your mid-sixties?

WALL: Sixty-eight.

LIEBESKIND: Sixty-eight. Clearly in any functional sense you're not retired. In terms of the university are you -- is the move over here a reflection of your age or something?

WALL: Well, I feel very, very strongly that mammals are supposed to have foresight and planning abilities and so on. And I have very little sympathy for those people who reach their retirement age and look aghast. So I really thought; I knew this was coming, assuming I lived. My father said, "You have to retire at the earliest possible time," which he did, at the age of 60, lived another twenty-eight years, having an absolute ball. I didn't follow him, so I retired at a compulsory age of sixty-five. But I really had thought about that before, so that for example, I was director of a research group with two exceedingly bright people, Clifford Woolf and Maria Fitzgerald [Professor of Developmental Neurobiology at UCL] -- so three years before I had retired, the three -- they were codirectors with me, or maybe even four years before. So they are now the directors.

Similarly with the journal *Pain*, I reckoned all sorts of reasons for sharing this with Ron Dubner. [Dubner, Chair of Biomedical Sciences at the University of Maryland School of Dentistry, served as editor-in-chief of *Pain* until 2003, when Allan Basbaum took over the journal.] So formal retirement means no formal commitment to a large group and so on. Fine. Space is very tight over there, where I previously worked at University College, and is not so tight here. It was just as convenient for me to move here [Royal College of Anaesthetists], thanks to Steve McMahon and this department [McMahon is Sherrington Professor of Physiology at King's College and Director of the London Pain Consortium]. So for the future I intend to do less every year, but by planning, not by surprise or orders from the outside.

LIEBESKIND: You have it under control, and you'll be able to stay here indefinitely?

WALL: I hope, I hope, yes. I mean, it may well be that the entire medical school collapses.

LIEBESKIND: There may not be any medical schools in the United States left either. So you're doing what you love to do.

WALL: Yeah.

LIEBESKIND: Continuing, and really, life must not have changed very much in terms of these --

WALL: I do less.

LIEBESKIND: When you say less, you mean fewer experiments?

WALL: Probably not. I probably do more experiments actually. And I've got all sorts of interesting things to do, to look at.

LIEBESKIND: What are you doing less of? Less teaching?

WALL: Certainly less routine teaching. I'm on various committees; I'm on the Council of the Royal Society and that sort of thing. But marginally less of the other things. I'll tell you a striking thing, this is by the way, which made me feel very suddenly old in a special way: There is a group of people set up by, triggered off by Rita Levi-Montalcini [(b. 1909, received the Nobel Prize in 1986 for her work on nerve growth factors, currently Director Emeritus of the Institute of Cell Biology in Rome] and Roger Sperry, who think that it's about time that somebody writes a Magna Carta of human duties. We've heard enough about human rights -- how about a Magna Carta of human duties? So they called together a fantastically distinguished bunch of Nobel Prize winners and a couple of other people, the two other people being [David] Ottoson [Swedish sensory physiologist, 1918-2001] and myself, and we sat around and talked about this and decided it was such a good idea we'd have another meeting. But then, being embarrassed by the obvious age of the people, we said, well, we really ought to have some young people. So for the next party in Trieste [Italy], it was asked, "Would you like to nominate somebody under forty interested in social responsibility?" So I sat thinking and I said, "I don't know anybody under forty interested in social responsibility."

LIEBESKIND: Do you know anyone under forty?

WALL: Well, the answer is yes, I do. So I went around and asked a lot of people, including a lot of people under forty, and I still can't find anybody.

LIEBESKIND: Times have changed, is your conclusion.

WALL: And then I suddenly felt old, I mean in an age package, concerned with things which younger people simply find some sort of silly ancient fantasy. That disturbs me. Age, nothing to do with physical age or the number of years -- it's being in a culture block.

LIEBESKIND: Well, not just any culture block, but in a block that you feel uniquely has a concept of social responsibility, lacking now in younger people.

WALL: Yes, as an example.

LIEBESKIND: It's very disturbing for the future of the human race.

WALL: That doesn't mean that I think that young people are acting irresponsibly socially, but that they don't consider it a topic for study, effort, activity, etc.

LIEBESKIND: There's no clarion call out there right now, is there? I mean, there's no rally point.

WALL: Not really. Lots of one-issue groups. Lots of "Peace nows" and so on, lot's of "No, stop its" -- "Don't put your highway through my back garden". [The Trieste group nevertheless founded the International Council of Human Duties at the University of Trieste in 1993 and wrote a 12-point "Carta of Human Duties".]

LIEBESKIND: Pat, you've talked a lot about students that you've worked with. You mentioned David Egger and on forward. Have they influenced you a lot?

WALL: Oh yes.

LIEBESKIND: Certainly as we look at your career, we see an awful lot of very prominent people today who have worked with you and were influenced by you.

WALL: Well, you know, I think, I was lucky at the beginning of being in with some astonishingly bright people -- I mean, Lettvin, Pitts, McCulloch, and I think to a certain extent they spoiled me, that I became a real elitist snob, that I really then wanted to join in with people who were smarter than I was.

LIEBESKIND: You couldn't find so many, could you?

WALL: True. But it means that I didn't make those bright people. I selected to join in with them. They were bloody smart characters before they'd met me. Don't forget also that most of the people that you would normally associate with me, weren't my students in the sense of being undergraduates and so on. At best they were PhD students who were already committed, identifiable characters, and many of them were -- Tony Yaksh or so on -- were already postdoctoral.

LIEBESKIND: Allan Basbaum?

WALL: Quite.

LIEBESKIND: I think there's quite a number of others who've come over in even more senior stages, people like Ron Dubner worked with you for a while, did he not?

WALL: Sure.

LIEBESKIND: Who was already well-established in the field.

WALL: Peter Hillman.

LIEBESKIND: Marshall [Devor], I guess.

WALL: No, Marshall had just got his PhD. That was a rather amusing story which he will tell you. He'd just got his PhD at MIT, long after I'd left, really working on neuroembryology -- and wanted to come and work with me in London. I really was relatively full in London, but I had this lab in Jerusalem, and I said to him, "I suppose you wouldn't like to go to Jerusalem, would you?" And it so happened that his entire family, I mean parents, were thinking of migrating too. So mother, father -- his father, unfortunately, died almost immediately, I think even before they moved. So they were from Toronto, Canada -- and his brother and sister, I think -- Any rate, the whole family moved to Jerusalem. And he was in a sense the only one with a job.

LIEBESKIND: Right. My next question might be too personal, but we talked a bit about the impact of your work, your career, on the field of pain. What about the other way, I mean, to what extent has your work affected your own personal life? You obviously have been very committed -- you've worked very hard. I assume it has been a great satisfaction to you.

WALL: Oh yes.

LIEBESKIND: Has it also been a problem that you have worked so hard?

WALL: No, I don't think so. I'm not terribly proud of myself in relation to individuals, such as two wives, but I really can't blame that on being too busy in the lab or things of that sort. I think the other way round. My personal difficulties, dissatisfaction with myself socially -- I was exceedingly happy to have occupational therapy available in the lab. No, I think those have been really fairly separate. I think that my self-respect, which was not very good as a result of personal interactions, was helped by, you know, honors and so on.

LIEBESKIND: What you've achieved. At the same time, you have been certainly a controversial person in the field, both because you have been first and because you have been iconoclastic, or whatever word we want to use for that. And this must have been difficult. I mean, I certainly -- your relationship with Perl, I remember in the early days being at some meeting -- I think it was the first meeting of the Society for Neuroscience back in 1971.

WALL: But you see, I've touched on that in that this clash of traditions and the example I gave of being summoned into that star chamber and being warned precisely that I came from, if you like, a class that could be expected to follow the classical lines, and I was clearly not doing so, not just in one way but in two ways simultaneously. So that this is not something to do with pain -- I do think that. Another thing that I've said, being committedly dissatisfied with the nature of society, the way society thought, being quite politically active at various times, so that I was not going to try to ooze my way into the system, I was going to fight the bloody system, and say so. Now, not many people do that. I see people with extremely new, exciting things, saying this in a very by the way, offhand way, hoping that they'll --

LIEBESKIND: Get through the system without being noticed.

WALL: Exactly. And I'd thought early on, it didn't fit my character. I didn't think one was going to get across a new line. And don't forget, initially really this was a marked failure. I mean, Lettvin, Pitts and myself, we were pariahs. So I was used to this. I don't pick a fight or like a fight, but I do think it's intellectually necessary, and I think there is another tradition that -- it may be completely unrealistic, but academic life to me should be open discussion, argument. In fact, everybody's ideas are their cherished children that they are going to defend with utterly illogical approaches. And one simply cannot say politely to someone, "That is bullshit; I'm sorry." I do say "that is bullshit" to people. That's with people who are illogically defending a line.

There's another bunch of real nudniks who just automatically churn out some answer as a supposed argument against you. I just lose my temper with those people, I -- and okay, it's

elitist and it's all the rest of it -- I'm sorry, don't have enough time left or never did have enough time for fools. Don't suffer fools gladly, and why should I? Now why should I? If I felt a threatened person who was going to lose my job and starve in the gutter, that's a good reason why you should keep your mouth shut. Thanks to parents, background, luck, et cetera, et cetera -- I never actually felt that way, so why shouldn't I tell a fool he's a fool? Especially if he's a pompous, pretentious one.

LIEBESKIND: Who would you count among your most worthy adversaries? I wouldn't ask you -- maybe I will ask you who you count among the fools, but who would you count among your worthy adversaries, who have you enjoyed fighting with the most? How about Peter Nathan? After all, he wrote an early article very critical of the gate theory, and so forth. Has he been a worthy adversary at all?

WALL: You see, the fact is that the people with whom I've been very close, we've had big arguments. I mean, Melzack, [Eberhard] Fetz [associate director for neurosciences at the National Primate Research Center in Seattle, Washington], [Lorne] Mendell [Chair of Neurobiology and Behavior at SUNY Stony Brook], [E. G.] Merrill [physiologist perhaps best-known for his development of tungsten microelectrodes] -- we've not had an easy, continually agreeable time. I count them as my worthy advocates that I respect. And not people who might be labeled publicly -- Perl, Iggo, Schmitt, Eccles, these people -- for whom I have a very low intellectual respect. They are hard workers, their experimental results are clever, difficult, and so on. Their understanding of the subject I have no respect for. And I certainly don't have any respect for their bulldozing the academic scene.

LIEBESKIND: I was just going to say -- you say their understanding of the subject is what you don't respect, but it surely must be more than that. It must be something about, as we were discussing before -- their approach, their quality of mind, the way -- I'm not asking you to comment necessarily on any one individual in that respect, but just in general. I have a question here: what are the traits in a scientist that you personally most esteem? What are the faults or flaws or weaknesses in a scientist that trouble you the most?

WALL: Well, you know, one criterion for this is you could define hell as being at a permanent dinner next door to "A". [they laugh]

LIEBESKIND: You could name a few A's.

WALL: That's right, I've just named them. And to a certain extent, a heaven would be --

LIEBESKIND: Who are people who are after all very sure of themselves, aren't they? I mean, that's not, that's part of the problem, isn't it?

WALL: Very sure of themselves and, I think, with a very limited repertoire of things they're willing to plug in.

LIEBESKIND: You know you're committed to your ideas. But would you say that you have stubbornly defended your ideas and not been open to looking at other ways? Surely not. You wouldn't feel that about yourself, would you?

WALL: No, no -- look, I've clearly been wrong about things. I mean, there were some experiments that were wrong. They weren't wrong -- well, they were misunderstandings of the situation.

LIEBESKIND: Being wrong isn't the worst thing, is it?

WALL: But the very way in which I've described my career -- I was beginning with a quite small, myopic, restricted area which I thought was good enough to explain everything that needed explaining. I was clearly wrong, have expanded somewhat. So right now I've got, let's just talk about mechanisms, let's say five degrees of freedom. I don't know the relative importance of those five, and even if they're all working simultaneously, they're not equally important.

LIEBESKIND: Figuring that out will take you into the next millennium. You told me about the '90s, now -- [they laugh]

WALL: Ah, yeah, but you see the real test there is: "To hell with what I am thought of by my academic colleagues." It's what the patients think of you that actually ultimately matters. And what it bloody well ought to be all about. So that I would love to see a patient with postherpetic neuralgia more comfortable. And I do think by manipulating those five degrees of freedom, they might be more comfortable. I just don't know how to do it. Or even prevent it.

LIEBESKIND: Pat, what do you consider some of the most important ideas in the field have been now in these years in which you've been active? Not ones that you yourself have been involved in, but that other people have been pursuing. Rephrasing the question, who else should I interview and why?

WALL: Well, obviously I'm doubting reductionism and keep on looking from, let's say, a cell to a system. Quite obviously, the people looking at chemistry of synaptic transmission, all of that sort of thing, are hugely important.

LIEBESKIND: Tony [Yaksh] is a good example.

WALL: Or -- you could still talk with him -- old (I'm blocking on the name) -- in Aberdeen.

LIEBESKIND: Hans Kosterlitz [(1903-1996), German-born pharmacologist best known for his isolation of the enkephalins, the first-known endogenous opioids, with John Hughes in 1975.]

WALL: Kosterlitz, right.

LIEBESKIND: Your friend -- your patient. I remember that trip back from Los Angeles.

WALL: True -- wow.

LIEBESKIND: He's still alive, I guess.

WALL: Yeah. I actually haven't seen him for a couple of years, but I guess so.

LIEBESKIND: He must hold the world record for the number of strokes that he's recovered from.

WALL: Yeah. So I think that's a level of people that I respect -- really haven't contributed at all to.

LIEBESKIND: Sure, it's been a whole other discipline. How about more from a clinical standpoint? What are the big ideas there?

WALL: For some reason in all of this we haven't mentioned Howard Fields [Professor of Neurology and Physiology at University of California San Francisco]. He's a guy that I enormously respect.

LIEBESKIND: Really. Why do you say that?

WALL: He really, I think, has scanned from the sort of physiology that I've been concerned with up to whole systems and patients. I'd certainly have him on your list. I haven't mentioned any surgeons who -- as I said, for Noordenbos' reasons, I wouldn't have put on the list.

LIEBESKIND: Yeah. I can't think of too many I'd want to interview. Sweet, well, he was there so long ago that I would feel an obligation to speak to him, get his tack, and he is obviously a bright chap, he keeps learning about new things, all the talk about peptides and so forth.

WALL: Well, that's true, yes. I think that, I mean, he was the student of [James Clarke] White, who really was in many ways a good old fashioned surgeon, with of course the concept of specific pathways to be hammered at. [White (1895-1981) was Chief of Neurosurgery at Massachusetts General Hospital (1941-61) and the author, with Sweet, of *Pain and the Neurosurgeon: A Forty-Year Experience* (1969).]

LIEBESKIND: I don't know, we've sort of gone through the questions in a sense. I mean, we've really touched on everything that I have.

WALL: I mean, of neurosurgeons, I do find [Jan] Gybels [Professor Emeritus of Neurosurgery at the University of Louvain in Belgium] a very interesting guy to talk to.

LIEBESKIND: Yes.

WALL: Psychologists, psychiatrists -- other than you --

LIEBESKIND: Well, I'm not a real psychologist.

WALL: Well, yeah. Well, go and talk with Melzack, but --

LIEBESKIND: I think [Wilbert E.] Fordyce has certainly been very influential in the chronic pain, the approaches to chronic pain. [Fordyce, Professor Emeritus of Psychology and Rehabilitation Medicine at the University of Washington, best known for his application of behavioral modification techniques to the management of chronic pain (1968)] That was very interesting, I thought it was very interesting to talk to him. Yeah, on that, I'm not quite sure where to go down that line. There are some younger people pursuing that.

WALL: There's a very interesting group here, very well organized and good. Every two weeks they take in six patients with chronic pains. Of course, mainly low back pains. This is National Health Service and they are quite interesting. And they stay here for four weeks.

LIEBESKIND: That's here at St. Thomas' Hospital?

WALL: Right. And so there are overlapping groups -- there are twelve people at any one time. They go home on weekends, assuming they have a home to go to. They have a separate room of their own in an old nurses' quarters, and they have a common room and they get their own food. I don't mean they make it, there are cafeterias and whatnot around. And then they spend the day doing everything -- a lot of talk, a lot of physiotherapy, a lot of behavior therapy, cognitive therapy, the works. And it's -- they're being very carefully studied and followed. And the answer is -- There are very few dropouts; most people make it through the four weeks. The answer is that this does nothing for their pain, but their amount of movement, self-respect, confidence and so on, is clearly way up.

LIEBESKIND: And their activity level, behavior, is changed.

WALL: Right. They are a very free and open group. They are fairly rigid about what they do and believe in things. So that the professional medical input is practically zero. We don't have quite the problem of the States of gross overdosage -- narcotic addiction and whatnot, although most of them probably are overdosed, so it is true there is some reduction of medication.

LIEBESKIND: When you say there's no reduction in their pain, how is that being measured? Do they complain less? If you looked at the different aspects of their pain, would their effective pain dimension have reduced?

WALL: No. If you give the McGill Pain Questionnaire -- the long one, let alone the short one --

LIEBESKIND: No change.

WALL: But that's not just at the four weeks. They've been looked at certainly in large numbers at six months and later, and the good thing is that their improvement is continuing, which is one of the very bad things about Fordyce's approach, where the evidence for that is not good.

LIEBESKIND: Really.

WALL: Apparently, yeah.

LIEBESKIND: A lot of recidivism.

WALL: Yeah. I mean, you can say that they are readjusting their standards of pain complaint. So they'll say, the pain is just as bad but it doesn't disturb me as much as it used to.

LIEBESKIND: Sounds a little like lobotomy.

WALL: Yeah. That of course was a -- I saw those patients way back, as I said, right at the beginning. Because there was this extraordinary business in the late '40s where there was an epidemic of lobotomy all over the world, and a much smaller epidemic of people saying, for Christ's sake, we better have a look at this. There was a huge Columbia [University] project called the Greystone Project [1945-49, to evaluate the effectiveness of lobotomy]. Greystone is a mental hospital, I think in New Jersey, just across the bridge [from New York City] somewhere. So I saw those patients. It simply isn't true that they were saying, "It hurts just as much, but I don't care." That their behavior was really moving so rapidly from one state to the other that if they said it hurt, they were acting as though it hurt, and since they were doing that every few minutes, and it's true you could distract them in between, so that I was never very impressed with that generalized statement: "It hurts but I don't care." Because I never heard one say that; it just looked that way, because the next minute they'd be doing something that seemed to be not a piece of pain behavior.

LIEBESKIND: So how about with these chaps that are being studied here? I mean, are their behaviors being changed? Are they being counted as failures of this program, this forward program?

WALL: No, no. It's interesting because of the changes in the National Health Service here, where there is a financial competition -- the patients don't matter at all, but the financial competition between various groups to treat patients in the cheapest effective way. I've forgotten what it costs -- I think it's two thousand pounds.

LIEBESKIND: For four weeks?

WALL: For four weeks, yeah, it's that. Now the alternative for these people, such as more surgery, would be so much more money that in fact the local health authorities are very happy to have this going on. Here's a booming part of the hospital, in competition with surgery and drugs and so on. Well, that's good.

LIEBESKIND: Well, that's good. Maybe when we get into more socialized and more controlled costs and so forth, that kind of thing can happen in our place. At the moment, they are paying for procedures still.

WALL: Right.

LIEBESKIND: There's no reimbursement to speak of for the kind of thing you're talking about.

WALL: There are some of these --

LIEBESKIND: Managed health care plans, that sort of thing.

WALL: [Hubert] Rosomoff has, for example, is an example of a place [Rosomoff, a surgeon, is Medical Director of the Comprehensive Pain and Rehabilitation Center affiliated with the University of Miami (Florida)] -- I think even in Seattle, where insurance companies or social organizations will send patients to those.

LIEBESKIND: I think those folks work very hard at -- the Rosomoffs and the Loesers -- work very hard at keeping their carriers convinced that, you know -- I think it's not without a lot of effort that they do that. [John Loeser was Director of the Multidisciplinary Pain Program at the University of Washington at the time of the interview.]

WALL: Yeah.

LIEBESKIND: As I've talked to people, it seems like it's a major problem in our country. I talked to a fellow not long ago, a young anesthesiologist, very well trained at Harvard or Yale and Stanford -- had a lot of good training, a lot of good pain training, and came to be on the faculty at the University of California at Davis. He was asked to be one of -- the second in command or something of their pain center. And he was complaining they were pushing him toward doing more procedures, nerve blocks, which he personally didn't believe were very effective. They needed that, those procedures done in order to get the reimbursement to keep their operation afloat. He said, "What am I supposed to do?"

WALL: Crazy. Tell me, there must be rumors going on, forgetting pain for the moment. Hilary Clinton was going to produce a plan in April, May, June, July -- are there any statements now? [President Bill Clinton and Mrs. Clinton were developing a national health insurance plan at the time of the interview; their proposals failed in Congress.]

LIEBESKIND: I don't know enough about it to answer you. Everyone is still waiting and waiting nervously, the medical community certainly.

WALL: There must be some rumors about what's going on.

LIEBESKIND: I don't know. I think people have gotten some reassurances, I think people are a little less concerned now in some ways, and I think that realistic considerations are coming to the fore.

Well, I want the interview to be open-ended. Have we neglected anything? I have a last question here -- what comments or suggestions do you have for me about this kind of an interview? What were the good or interesting questions, what were the poor or dull ones? What other questions should I have asked? So the ball is in your court.

WALL: I tell you, there is a book called *The Encyclopedia of Ignorance* [Ronald Duncan and Miranda Smith, 1978] and it has a lovely story associated with it. There was a teenage girl, now in her twenties, who came from some ludicrously intellectual family, so all the people coming into the house would always ask her, "Well, I suppose you are going to the university, what are you going to do?" So she said, "I don't know." What sort of answer is that? So this smart girl, admittedly with the help of a poet friend of the family, wrote around to everybody they could think of, asking them: "What don't you know?" Her idea was that the most interesting answer would tell her the subject she was going to go into. Any rate, so people replied to this girl quite seriously.

LIEBESKIND: This is a true story?

WALL: Oh yes, absolutely. And so they put these answers together and it's published -- two volumes. There is hard sciences and life sciences. Published by Pergamon [Press]. And it's fascinating.

LIEBESKIND: Did you submit -- ?

WALL: Oh yes.

LIEBESKIND: Oh you did. Well, then, there's obviously -- [they laugh]

WALL: It's somewhere in my bibliography. But the reason I bring it up was if you look at the book, it was fascinating to see how many people could not answer that question. A lot of them said, "I've worked my way through the alphabet in my academic career and I'm up to P, so now I want to study the thing I don't know, what is Q." And those of course were deeply boring and one felt very sorry for these people. There were the interesting people who said, "Well, I've gotten to this stage, and now I know what I don't know, but even more important, I know why I don't know it." So that's what you need to ask people in these interviews: A, what don't you know and why don't you know it?

LIEBESKIND: How would you answer that then? That question that you posed?

WALL: So why don't I know it?

LIEBESKIND: First, what is it that you don't know?

WALL: I don't know how the brain works. And I suspect that --

LIEBESKIND: Of course, you do know how the spinal cord works. The brain is just your key.

WALL: Just because there's a foramen magnum [the hole at the base of the skull which allows the spinal cord to pass through and connect to the brainstem], I don't separate the brain from the cord. I always regard the spinal cord as the queen of the brain. The brain's just collecting and sorting the information and telling the spinal cord what [to do]. I think I do know how the CNS works, I mean, the peripheral nervous system works -- nothing to do with me. I think there is a

spectacular and enormously satisfying intellectual thing that we really do understand a nerve fiber in huge detail. We really do understand an action potential.

LIEBESKIND: Once they start talking to each other, then we're in deep shit.

WALL: Exactly. And I do not think that we know yet the language. I think we are just beginning to discover some of the phonemes in the language, and not even all of those, and I think we've got to.

LIEBESKIND: Are you as confident today as you were when you were younger that it's knowable, that we will get there? Somebody gave me a quotation once, something about the human brain -- if people were smart enough to understand the human brain, let's see, no --

WALL: You see, I know the rules of chess. I'm a lousy chess player, but I know the rules of chess. So that I would like to be able to get to the stage of the brain, which I think is surely possible, that one knew the rules. That doesn't mean to say you know how it's playing the game. So I think at least, and I don't believe we know the rules which are being applied. And I think if you were to observe people playing chess, you would be able to define what the rules are, even though you didn't know how they won or lost. At least that stage would seem to me to be achievable.

PATRICK WALL INTERVIEW

TAPE THREE, SIDE ONE

WALL: What are the rules of the central nervous system which we don't know and why don't we know them? It seems to me to be quite clear that there are long-distance interactions between nerve cells, and we simply do not have the basis for that. We degenerate into hand-waving and ho-hums and all say, oh well, that's all explained by action potentials running from here to there, which I don't believe. And why we don't -- for example, precisely what I'm doing at this moment, which is waving my right and left hands in some sort of concert, not independently, how my right and left hands are
cooperating and, if I were to pick something up with both hands, would be cooperating. We simply do not have the ability to move to that stage. And the reasons are that we don't even know that this is a problem is [that] we are very bad at multi-unit recording. Great at single-unit recording, really rather good at single-cell morphology.

LIEBESKIND: When you say multi-unit, you mean two single or multi-single units at the same time, not from one electrode?

WALL: Exactly. And there are all sorts of suspicions that there is some medium of talk between these things. And some suggestions for what it is -- slow waves and so on -- all, by the way, on a larger scale coming back to a much larger psychology like gestalt psychology, suggesting these long-range interactions and lots and lots of biophysics and so on, suggesting this. It seems to me to be quite crucial as a next step, defining what sort of technology you'd need to define the phenomenon and what sort of things you might investigate. Now, that's not going to explain the brain or explain beauty or pleasure or something, but I see that as a fascinating next step, so that I would adore to read *Brain Research* in 2050, to see what they're talking about. I don't think they are going to be explaining beauty, but I think they might take that sort of interaction absolutely of course.

LIEBESKIND: Would it even be possible to read it fifty years ahead with our vocabulary?

WALL: That would be interesting.

LIEBESKIND: We'd probably need a lot of new schooling, wouldn't we, to know what the hell they're talking about.

WALL: Yeah....you know, Helmholtz [Hermann von Helmholtz (1821-1894), German scientist who worked in both physiology and physics, and made important contributions to our understanding of acoustics and optics.] would understand what we're talking about today.

LIEBESKIND: Even if he didn't know certain of the terms or certain things.

WALL: Sure, no, I mean, some of it would be written in the new language, but there wouldn't be any fundamentally new concept in there. Fascinating ways in which you hear in Helmholtz's

sense of hearing. No, it's true. You or I, certainly I, look at *Science* and I don't understand the title of most of the papers, let alone the content of the papers. But that's because they're talking in jargon and I just haven't caught up with the language.

Crikey. Look at even in our own subject, like neuroscience, you look at the sudden appearance of NO [nitric oxide] -- suddenly appears all the way through half the articles -- you know, what's "NO"?

LIEBESKIND: You realize it's been there for ten years and you haven't been following it and now your friends are doing it, and what is it all about?

Well, gosh -- I think in a couple hours we don't capture someone like Pat Wall, but I feel very good about this interview. I feel like we've not only traced some of your own intellectual development, but had little glimpses of who you are, and there seems to be a oneness about it -- I mean, whoever you are as a human being, that's what we've seen in science, too.

I remember one chap I went to graduate school with and meeting up with him years later at his university. And we were at his home, and he was very -- just like old times and so forth -- and we chatted and had dinner and I stayed at his home. The next day we had breakfast and then he wanted to take me to his laboratory and as we entered his building, it's like a cloud fell in front of his face and he seemed transformed. He became like a monster -- I mean, he just seemed very different from the same -- who he was when he was not at work. And I had heard filthy stories about him, what a pig he was around the lab. But with you, I get that you are -- I mean, these values that you have and so forth, in the rest of life, are also seen in the way you approach your science, and that you are sort of a unity.

WALL: Well, maybe. I think, on a practical level, there is the question of what to do with tapes like this.

LIEBESKIND: Yes.

WALL: There's a very good chap here who actually has written an almost daily thing in one of the papers in which he interviews people in this rather open-ended fashion, but he extracts with great skill.

LIEBESKIND: Well, that is the skill, isn't it? Anyone can turn the button on.

WALL: And I'm sure -- I mean, he's done it to me, and although he was giving maybe one percent of what I said, or five percent or ten percent, I thought it was absolutely legit. And sure, I'd said more than he reported, but --

LIEBESKIND: Well, I do accept the challenge of trying to do something with these tapes and all these interviews. I would like to do a book that will extract these things and talk about the development of the key ideas in the field of pain. But first and foremost, I am creating an archive which others can use and make their own extractions from. We all know that two

different historians could look at the same material and come up with different things about it. So these are going into the public domain, as I assured you in my first letter, and so forth.

WALL: Very difficult. There was an anthropologist at Harvard in the '50s [John K. Marshall (1932-2005)] who happened to have a very rich father who owned Westinghouse or something [Raytheon] -- and his father said, "Great. Anthropologists, they go on expeditions. I'll finance your expeditions." So this chap went off to look at the people in the desert in southwest Africa [the bushmen of the Kalahari desert]. So here was an isolated tribe, absolute great meat for anthropology. And this chap with his father's money, said, well, sure, I'll go and make a study of these people, but why don't I take along enough recording equipment and photographic equipment that we will make documentaries which other people can make use of. And they did a fabulous job. And they took this bunch of people, whose name I will think of in a moment, and said, well look here, these are hunting people. So let's photograph everything to do with the hunt. And of course three-year-old kids are chucking stones at things, that's part of hunting.

So they really did a fabulous job of picking out fractions of the society and taking pictures, one of which was called "The Hunters [1957]." They are great documentaries, won lots of prizes. I think partly because of this, they picked a theme and photographed it in the fullest detail they could and obviously -- food gathering and house building and whatnot -- not that these people had many houses. Whether it worked -- whether an anthropologist now forty years later could go and get something new out of it -- I doubt very much, because they'd now be wanting to know, what was that man saying to this man, and that wasn't recorded.

LIEBESKIND: So you're saying, it's not -- I mean, what we've done here today in whatever, three and one-half hours or three hours, is to take a particular slice through Pat Wall, and someone else could come in here a week from now or have done so a week earlier and they, by dint of the interaction and the questions that were asked, would have gotten very different material and the historians looking at those two sets of three hours' worth of recording would see very different things.

WALL: Right. I mean, to take a silly example, you haven't asked me my birthdate, so you don't know my astrological sign. But there's an example where a culture could be saying, let's look at scientists in --

LIEBESKIND: But that's a matter of record. That's the kind of thing I really don't care to go after.

WALL: Okay.

LIEBESKIND: You said it was a silly example, but my question is, are there questions that I should be asking that aren't easily found out and aren't a matter of just record? I mean, for example, just when I was planning my interview and thinking a little bit the other day about my interview with Dame Cicely, I realized I really don't know very much about her and so my father-in-law in Charlbury [near Oxford] there, said, "Well, why don't you go to the library?" I said, "Well, anything they have in the library is not what I want." That's not -- you know -- I want to know.

WALL: An entry in *Who's Who* which you write yourself is interesting to see what the people have picked out.

LIEBESKIND: Okay, but that can always be gone to. But I'm interested first and foremost in the ideas; but I'm interested in the person in relation to the ideas, and I don't think any of that would come out in an encyclopedia.

WALL: No, but I do think that – See, even a social psychologist might have said to me, look here, you have spun out this story as though this was you moving by free will along some path which way you've made all these logical steps. Are you serious that nobody ever came up to you, in fact, and said, change tack? That's not something someone volunteers usually. I talked about teachers at the beginning who certainly dominated me in, I think, a good way, and a few I could mention who I've thought did the opposite.

Of course, it could be that someone would like to spin a line, like who was my mother or who was my father or something that, ah, we can see causal relations here. Maybe that's been overdone. But I would have huge difficulty in honestly unraveling the importance of, let's say, Lettvin and Pitts, who were hugely important to me, I'm sure -- how free was I, how much did they bend my mind, and so on. They certainly did bend my mind and to a level where I wasn't happy. And happy to go off and find something they weren't working on or had given up as being insoluble.

LIEBESKIND: What do you mean by that -- that they were intimidating in some way? You were glad to kind of --

WALL: Oh yes. So bloody bright. And bright with the sort of line that you'd have a flaming argument one day and think about it overnight and go back the next morning and start up -- they'd forgotten the line they'd taken and were taking a third line which --

LIEBESKIND: Or your line! [they laugh]

WALL: That sort of thing, yes.

LIEBESKIND: How do you rate a career such as Jerry Lettvin's? He's very well-known for the frog work, but not for so much else, is he? I understand he was a brilliant chap. How much did he -- has he affected the world very much? Not as much as Pat Wall has.

WALL: There I think you have the question of -- I think clearly you can be so bright that you can see all the pitfalls of not proceeding, that there isn't going to be an ultimate answer at the end of this road, so quit.

LIEBESKIND: Is that what he did? Did he basically quit? I don't really know much about his career. Did he continue to be productive?

WALL: Very much in influencing people, a brilliant writer and talker about all sorts of things.

LIEBESKIND: Is he still alive?

WALL: Yeah.

LIEBESKIND: Did he stay at MIT all those years?

WALL: He stayed on at MIT. I'm actually out of touch just recently, like eighteen months or so. He is of course way beyond ordinary retirement age. Rutgers offered a sort of a think tank position, so he moved at least part of the week there. He and Pitts were similar in some ways, that an hour's conversation with Jerry or about five minutes in the case of Pitts would set you up for a year or two.

LIEBESKIND: Can you name others who were influenced in that way by them? I'm asking really, how do you --

WALL: I think a whole generation of MIT undergraduates were made to think, doubt, seek, shake and – but I'm going to see one of them tomorrow.

LIEBESKIND: From MIT? Someone from that group?

WALL: Yes, a guy called Hentall, who actually worked with Fields after that. [Ian D. Hentall, now Associate Professor of Physiology at the University of Illinois College of Medicine] I mean, so there's somebody at a distance looked to be undisciplined, a butterfly.

LIEBESKIND: What would his [Lettvin's] CV look like, or doesn't that....? That doesn't measure the man, I know, but --

WALL: I'm sure small numbers of published papers, because by the time he'd got around to thinking of writing, he'd thought, why, the whole subject was nonsense.

LIEBESKIND: I myself feel concerned about how topics come and go and how we don't -- I guess I worry that we really do learn anything of lasting value and sometimes I get very concerned about that, that we work away at something. I think of some of the topics that my lab has been involved in. They're just, they're gone -- it's just, people aren't doing that anymore.

You talk about going from A to B to C, well, now I'm up to Q, well, we did stimulation-produced analgesia and stress-induced analgesia -- what do we really know about things like that? Is it iterative? Does it really -- ?

WALL: Oh, I wouldn't run that down at all, because -- no, no, in terms of permanence, because I think those were -- I mean, I should have mentioned that it was a hugely important and permanent step, showing a plasticity of the nervous system, i.e., that even very simple responses, tail flicks and whatnot, quote "simple responses" in quote "simple animals", are astonishingly modifiable in very subtle ways. It wasn't obvious before you started.

LIEBESKIND: I guess I don't see all the continuity, and I don't see that fifty years from now or even five from now, anyone will necessarily really remember any of that work.

WALL: True.

LIEBESKIND: Or that it will have led, you know, A led to B which led to C. I'm not sure. I don't feel confident. I don't mean just -- I'm not just talking about my field, but more generally.

WALL: I'm sure you're right that you could republish your papers of twenty years ago now, changing the odd word here and there, and they would appear as utterly new, because people hadn't read them. Their computer searches don't go that far back. But I think in terms of a step which then is completely accepted and in the culture. I would have said you've made many, and you mentioned two, as an example.

LIEBESKIND: Well, again, I'm not here today concerned about me, but I am concerned about the field of pain and whether it is, whether in your view it's iterative and it's moving forward, and things are building on things.

WALL: As I said, I would really like to see the field disappear, and I think intellectually it should disappear. It seems to me that to pick pain as a specific topic has no more logic to it than picking the color blue out of all colors, except that it happens to be that people complain of pain. There may well be some animals around who hate blue [they laugh] and that blue to them is the same as pain to us. So that in the sense of a concatenation of events which we hate and call pain, I will be very happy to see that generalized in that sense.

LIEBESKIND: But it's only by focusing on it that we bring people together. We come together.

WALL: Now, that could really be an intermediate stage.

LIEBESKIND: So then it would go back to physiology, let's say, or something, is that what you're saying?

WALL: Yes. I mean, if you take the whole sensory system, for example -- how are we aware of what's out there and what's inside us -- it may well be that there will be long periods of time when vision is running with it and audition at other times, and then people settle back and say, no, we've got to decide what's standard, how you make a standard, how do you call something zero.

[INTERRUPTION]

WALL: If you take the topic of pain, intractable pain, I can believe that a series of maneuvers could appear, either because, let's say, arthritis becomes under control, something of that sort. Or what I would be most optimistic about, where nerve damage becomes under control, where as a problem the thing disappears, leaving behind you the intellectual question, what the hell was it anyway?

LIEBESKIND: By the way, how does pain work, in respect to pain? [they laugh]

WALL: Exactly. I think, by the way, this is a horrific example which you see in other aspects of clinical medicine, when you say, well, there are poor children with Duchenne muscular dystrophy [a disease characterized by progressive muscle weakness and wasting, linked to a recessive gene on the X chromosome], and now that we know the DNA sequence, we understand that perfectly. That is a little bit wrong on.

LIEBESKIND: Gene so-and-so, whatever, chromosome.

WALL: Exactly. And that's it. That's what Duchenne muscular dystrophy is. And conceivably you might be able to take these poor children and stuff another gene in them and you'll never know what the disease was, although they will be perfectly satisfied that they now understand the disease.

LIEBESKIND: Just coming to the end of an interview. We've been talking for [three hours].

WALL: Entirely about me -- lovely, my favorite subject.

[MARY] McLENNAN: Well, carry on.

WALL: We're going to rerun the tape.

LIEBESKIND: I forgot to turn it on! [they laugh]

WALL: This is actually the interesting question of what do you do with verbal history, you know -- not entirely a rambling interview, but a pretty long interview with somewhat --

McLENNAN: Well, historians are much more interested in an oral history now.

WALL: Right. But they of course condense it.

McLENNAN: Well, they pick their own particular standards, don't they?

LIEBESKIND: Well, this part of the conversation started by my saying that what I plan to do with these series of oral histories or interviews, which are minimally two hours, maximally four or five hours, I suppose -- is to, first of all, make them available to others, so that here they are, here are the tapes, here are the transcripts of the tapes -- you listen, you decide what's there. Beyond that, I myself would like to do a book that would be based on this information. So my thought was, the facts are the tapes and the transcripts of the tapes -- that's the raw data. Now I'm going to put on my particular set of colored optics, whatever, and look at those, listen to them and interpret history, make, write history as I see it.

McLENNAN: Right.

LIEBESKIND: But what Pat pointed out, and I think he's absolutely right, is that even the data are not raw, the data are not pure, the tapes themselves. This interview has been affected by me, it's been affected by what side of the bed Pat got up on this morning, it's been affected by the questions I came in with, and someone could come in next week and ask a very different set of questions, be nasty, let's say, with Pat in some manner, or challenge him in some unpleasant way, provoke other kinds of answers and get off onto different kinds of things. If the same historian who listened to the tapes that we've done here listened to those, they'd have a very different view of Pat Wall and the issues in the field of pain.

McLENNAN: Well, nothing can be ever that cold.

END OF INTERVIEW