PAPEZ MEMORABILIA: PAUL MACLEAN

recorded at Potomac Maryland, February 1-2, 1981

- K.E.L. I am interested in your first contact with Papez and what happened after that.
- P.M. My recollection is that I went to the library looking for an article by Marshall and Saul in the Archives of Neurology and Psychiatry Saul was later an analyst. As I recall I found the Papez article on emotion in the same volume and was absolutely fascinated with it terribly excited.

What I was after in particular was some idea of how the different sensory systems carrying feeling could get into the hippocampus. These were cortical - cortical things to be sure but it was important to have a hint as to how this information might be feeding into the hippocampus.

- K.E.L. You were with Stanley Cobb at the Massachusetts General at the time.
 Did Stanley Cobb know Papez personally at that time or did he just know who he was?
- P.M. Oh, he knew Papez. I had the feeling at that time that the "leaders" in Neurology recognized Papez as a person with a lot of information and knowledge, but also as a little bit "touched". He just didn't quite fit in. There was the sort of feeling that he didn't quite make it with the real Eastern Ivy League. If you were a little away from the East Coast you were not quite with it, not quite in the center of the world. Having been in the interneship competition for hospitals on the East Coast myself I was very sensitive as to how that system works. If you were too far away God help you!
- K.E.L. After you found that article in the Archives you talked to Stanley Cobb about it. Was he the one that suggested you go and see Papez?
- P.M. As I reconstruct the thing what was bothering me, working with these patients of Stanley Cobb with epilepsy psychomotor epilepsy we were recording basal electroencephalograms with these special nasopharyngeal leads and leads placed right against the tympanic membrane. We thought we were getting activity from the fusiform gyrus and hippocampal area. This group of patients would have all of these different sensory experiences

in their auras-auditory, visual, somatic sensory, visceral sensory - all sorts, where was all this coming from and how did it get to that basal area?

Originally with my interest in Psychosomatic Medicine - the thinking was that everything went on in the hypothalamus. So I wanted to record from the base of the brain near the midline to get something from the hypothalamus. Hudson who was head of the Worcester Institute brought Voegelin over when I was working with the new style nasopharyngeal electrode. They were simple and easy to introduce and we got nice quiet recordings. But I discovered that I was umpty-ump centimeters away from the hypothalamus, but quite close to the medial parts of the temporal lobe.

That is something I haven't been able to reconstruct - how I got into this recording thing in patients with psychomotor epilepsy and became so fascinated by their symptomatology. It was in '47 and '48 - I was there with Stanley Cobb for two years. I ran on to the Papez paper pretty early in '47, I think. Knowing what an ignoramus I was about everything - especially in electronics. I can't imagine looking back how I got into that as quickly as I did.

I was in Bob Schwab's laboratory at the time. They were a great bunch. You were just steeped in this EEG stuff - completely surrounded by it.

- K.E.L. When you talked to Stanley Cobb did he suggest that you go to see Papez?
- P.M. I think I went to Cobb with sort of an antomical question "how about all of these sensory things in these patients-visual auditory etc." I talked about Papez article, and I guess Cobb must have said "why don't you go up and see him"?

Looking back at my own diffidence about anything mechanical -

It wasn't that I hadn't done things with my hands painting and that sort of thing, but that whole
business seemed out of character for me. I never
did like that part of medicine - the anatomical
dissections and the experiments in physiology feeling that sticky flesh - that whole business
was out of character.

I think I was just terribly driven by curiosity to try to find out what the hell was going on up there. Just as the war had opened up up my own noggin - that the mind has to be up there in the head. was really my rationale for going to medical school orinally. I had been planning to study philosophy in Edinburgh. During that first year I had this sort of last minute conversion to go into medicine thinking that learning about what goes on inside the cranium would be one of the invaluable fall-outs of that medical experience. But when I finally got into medical school, it was all sort of reflexology as far as the brain was concerned. So I sort of came to the conclusion that the mind wasn't in the head since I couldn't get any interest or support for that idea. Originally, I had planned to do my thesis in neurophysiology but I ended up you know in Winternitz's department working in the cardiovascular system. It wasn't until World War II that I finally got back on this track again through interest and exposure to psychiatry.

- K.E.L. When did you enter Medical School?
- P.M. Well, I didn't really have the requirements to get into medical school.

 So when I went to Edinburgh in '35 I took physics and chemistry there and came back in the summer to finish with organic chemistry at Cornell.

 That was the summer of '36 just before Medical School. Chemistry was so terribly taught at Edinburgh it was just awful. But I had this teacher by the name of Johnson at Cornell who was great. I just couldn't help getting 100s all the time. The biggest surprise was to find organic chemistry easy just the reverse of what I thought it was going to be.
- K.E.L. Then you came back to enter Yale Medical School in the fall of '36?

P.M.

Yes, and finished Medical School in '40. Then I went to interne for a year at the Hopkins, and after a year there came back to be an assistant resident at Yale with Frances Blake in Medicine. After that I was to go to Boston to the Peter Bent Brigham to work with Soma Weiss. He was a wonderful man and a wonderful teacher. At that time he was one of those absentee landlords - going back and forth to Washington in those early days before we got into the war - to consult with people down there. On one of his visits in Washington he developed this sudden terrible headache. He knew what it was and diagnosed it himself - a ruptured Two days later he was dead. A terrible blow. aneurysm. With the death of Soma Weiss and the war coming on the next thing I knew I was back at Yale - Winteritz was there at the time. He was a very determined person. He was getting into gas research again. I remember he was trying to persuade me to stay in research and forget this business of signing up and going into the Service. George Smith who taught me bacteriology at Yale was a friend of mine - he had gone the research route in the first war and had always regretted it - that he hadn't "done his bit". But for the first half of that year I gave up my assistant residency in medicine and went into war gas research with "Winter". But I signed up with the Yale Unit the 39th General Hospital. Quite late in the latter half of that year I ran into Allison and began dating her. She was much sought after. Thursday nights were the least popular, so that is when I would go out with her. That was early in 1942, soon after Pearl Harbor.

In the 39th I went in as a bacteriologist. Avery Lebold was my supervisor. When we got to Aukland our hospital had not been built yet. The New Zealanders kept assuring us that it would be done in a fortnight. But as we discovered a fortnight could be two weeks, two months, or two years. We were bivouacked out in this lovely farm country south of Aukland with skylarks all around singing to us. But it was just such a God awful collossal bore just sitting around there week after week. It became almost like being in prison. Dave Crocker in our unit had graduated with me in medicine. I had been persuasive in getting him to join the 39th. Steve Corey an undergraduate classmate came in as Chaplain. He and I had gone to Edinburgh together. He was to get his Divinity Degree and I was to study philosophy with A. E. Taylor, but I changed that and did physics and chemistry.

Anyway, Dave Crocker (who later became an analyst in Cleveland) and I found that they needed some help with the Navy. They had temporary quarters on a cricket field in Aukland, so we went in there as volunteers. David was going into psychiatry and latched on to this Navy Psychiatrist whose name escapes me just now. At any rate the poor Marines who had come down from Guadalcanal had been shelled for six weeks in a row with six inch shells. They were literally eating rice and maggots. They all had malaria and jaundice with great big livers. They came down with glass bottles full of Japanese ears and gold teeth, that they kept under their beds. Everytime a plane would fly over they would hit the deck. They were just terribly sick physically and psychiatrically all shook up - so that was my real introduction to psychiatry.

When our hospital finally did get going I was in bacteriology. Averill Liebold and I got interested in the tropical ulcers - "jungle rot" trying to culture something out of them. They had had all of these tropical medicines applied to them. Averill gave them first saline soaks and after that we tried to culture the wounds. I was surprised to find that Averill really didn't know one bug from another. At Hopkins I had had a month in bacteriology - quite a good course. So with his going about it that way and through the little bit of knowledge I had of bacteriology we cultured-out these organisms which turned out to be carinea bacteria - one of the diphtherias. So once people knew what the problem was there was a method of treatment. A lot of these fellows and patterns of stocking anesthesia which everyone assumed were hysterical. These were sent back as psychiatric cases, though they had these partial paralyses of their pharyngeal muscles as well.

K.E.L. - Was there a specific treatment for the neuropathy and "jungle rot"?

P.M.

We didn't have anything specific at that time. That was when I began to work on some pseudomonas - the bacterium that grows in the tars and oils around garages. Mechanics never get infections on their hands. This organism produces a secretion that is bacteristatic or bacterocidal. So I made this brew from the blue bacterium which we could apply. It was bacteriostatic. One Nurse I remember had this bad fungus on her hands - terrible - she just couldn't get rid of it. I made a salve for her and she had an almost overnight cure. They had medical rounds and I presented this stuff. They called it MacLean's magic and then MacLean's quack medicine. But then just shortly after that penicillin came in and we were out of business.

But I had written Francis Blake who was then in Washington. He was very interested, but almost overnight I was out of business because of pencillin coming in.

- K.E.L. That probably helped to get you back on your other track.
- P.M. Well it was not long after that when I was working in the bacteriology lab, I discovered I could never get my microscope clean. At first I thought it was the eye piece, but it wasn't. That was the beginning of my trouble with the eye.

At that time lots of casualties were coming in from the Pacific. A third would be surgical, a third malaria, and a third psychiatric. Convoys of patients would come in - 1,000 at a time. The hospital would fill up and then be empty in a week by transfer. All of our psychiatrists like Warren Brown and one other person had moved up into the administration. They really didn't have anyone doing psychiatry, except Merrill Moore, the Sonnetist and Psychiatrist. He was the only one left for these thousand patients. Crocker was helping him out. Then Crocker realizing that I had had some exposure to psychiatry during those weeks with the Navy brought be on board. Moore and Crocker were interested in the psychoneurotics so they put me in charge of the disturbed ward - the psychotic patients. So that was my real introduction to psychiatry. At Yale I had never worked with psychotics at all.

I began with that experience to feel increasingly certain that the mind must be in the head. Much to the disgust of my colleagues I made up these questionaires and had the psychotic patients fill them Dave Crocker and I wrote a little piece "Why Soldiers Break Down" or something like that. You see in the South Pacific 20-25% of all our casualties were psychiatric - 23% I think was the figure. In other theaters psychiatric casualties were not that high. So there was something about this jungle warfare - the fox holes, the kind of enemy they were fighting, the jungle itself etc. There were even stories that there were Japanese women in uniform. One soldier I saw was all shook up because he had shot this sniper down from a tree, when it landed the shirt fell open and there was a breast - a woman. That is what he reported. It could have been fantasy. The Japanese would place Gillette razor blades in the trees, so if our soldiers climbed up they would get terrible cuts. It was a little time before the word got around. The soldiers found this was one of the hazards of climbing up for a coconut, or to look around to see where they were. So it was kind of wild.

We would get people from the air corps - pilots coming down for rest and recreation leave. The Air Forces idea of rest and recreation was to provide all the booze and women they could take. They came down after flying 50 missions. After they went back to duty following one of these rest cures, we never heard of anybody who really made it. They would go - back and just seem to disappear. Their planes would just seem to blow up or disappear in the cumulus clouds somehow. Very few seemed to last beyond the 50 mission cycle and the rest cure.

P.M. - My eye during this time got worse and I was invalided home because of the uveitis. I landed in San Francisco and took the Santa Fe across the country to Atlantic City. Then through the agency of Bayne Jones, I think, they got me into the Valley Forge Hospital where there was a good Opthalmologist. The treatment in those days was diathermy - they also used hyperthemia. They put you in one of these oven tents that cook you

at 120° F. until you develop a good fever, then they would give you morphine. Talk about hostages and torture chambers - the hot box was a good one. Then the morphine. I don't normally get sick on medications but that combination of heat and morphine made me puke all over the place. It was terrible. Then they skin tested me for tuberculosis and I had a little hemorrhage in the vitreous after that. I suspect that if I hadn't had so much medical attention and had been able to stay away from physicians, the uveitis would have run its course in less complicated fashion. In New Zealand they looked everywhere for a focus of infection. They pulled all my wisdom teeth. I think if I had stayed in New Zealand I wouldn't have had much more - maybe a toenail or something, but I exchanged that for all these other tortures.

I was 43 then. They wanted to retire me. I remember going for a consultation in Aukland with Freddy Weese who was the Ophthalmologist in our unit. The consultant was a nice older fellow with silver gray hair like a physician. But I was just the object - he said "how old is this trouble?" "yes, and how old is the patient?" We told him and he nodded and said "too bad, he is such a promising young man - yes he is going blind in this eye and later the other". Jeepers, it was awful waiting, as I went slowly blind in that eye and was waiting for it to catch the other one.

Anyway I said I wasn't ready to retire. So instead they sent me to Brooke General for a year in San Antonio. I worked there and also had 6 months bed rest treatment. They decided I had tuberculosis of the eye. So the treatment was bed rest and no reading for 6 months. Allison read to me for a whole year there. I nearly went nuts that year. If you are an active person being in bed is like a straight jacket. You are so helpless. Even the part of being read to was driving me straight up the wall. I am a somewhat aggressive person wanting to do things and be active, so I became all bottled up inside - almost a raving maniac.

After Brooke General they wanted to retire me and give me a pension. I

refused. I had this guilt feeling that I had gotten out of the war through

this damned eye thing. 'That the illness was somehow my fault because I had wanted "out". That is one of the "advantages" of being a Presbyterian. I wasn't going to be remunerated for it - so I got out without any pension which I could have had at that time. I'm glad I didn't have it because every dollar in your pocket that you don't have to work for depletes you a little. Later, though I am not so sure of all that because it has been great to have a bit of extra support to be able to stay in academic medicine and do a bit of research - that has been a great luxury.

After I left San Antonio I went into private practice for a year in Seattle and then came back to Boston. I really didn't quiet down psychologically until I became completely blind in the right eye. I remember that slow decline - I was seeing a little less and would test myself each time I went out driving in Boston, particularly at night. The other thing I discovered is that you can get a picture of the opacity lens reflected in your glasses and watch it grow.

I remember my ophthalmologist Dempsey saying "Paul you just have to get used to being a one eyed individual". He didn't hold out any hope for contact lenses or anything. Some people can't tolerate them of course so it was the greatest surprise when I did have the opaque lense taken out in 1961, that that wasn't necessarily so. Malmony who was younger just took it for granted that you would wear contacts. When I first put it in I was amazed except that I was 30° out and 10° down. shift had begun earlier. I remember in 1957 when I was reading in the library in Zurich I would come home at the end of the day looking like Ben Turpin - my eye was rotated so badly. I really got badly cross-eyed that year. Then I had a tuck taken in the external rectus - wow, the next morning I was 40° off! Even Malmony wondered for a moment if he had done the right tuck! Then we went off to the Bahamas. I was still right eye dominant and I damned near killed myself driving the car. I would suddenly see this car coming right down the center of the road at me and I would make a sudden turn to the right! But after two operations I said no more surgery. Although they were promising they could help me, I just worked on the thing myself.

Now except for a fatiguing day, or one cocktail - not several just one! Alcohol is great for the synapses you know. It is a good litmus test for drinking. Anyway with fatigue or alcohol that right eye will get disinterested and go "off" - except for the microscope. That is the only place I can drive them back together. I am only a one-eyed person through the microscope. I use it a lot. That is the way I relax at the end of the day. Once you have done any extensive work with the microscope, for example doing neuroanatomy, it is like going through a lovely museum someplace - an esthetic experience looking at stained tissue. And even with one eye I get a stereoscopic effect just from the way the fibers are streaming and so forth.

- K.E.L. Was that situation with your eye stable in 1946'47 when you became interested in Papez?
- P.M. Oh, no, we were still in the midst of sorting that out. I was supposed to see Dempsey twice a year but things got so busy the year John Fulton died I missed my check up. So I went to see my friend Don VonAlten here at the Eye Institute. He announced to me that I had a high pressure mature cataract and had better get over to the hospital as soon as I could. Wow, the day before I had been out riding "Pumpkin" (the horse). He is a great shier. If I had had a fall and that had ruptured wow! That was the year that we signed over the Journal of Physiology to the Physiological Society. John Fulton would have turned over in his grave, but I didn't see any other way to do it to keep the thing alive.
- K.E.L. Now to return to the Papez visit. You were driving with Dr. Arellano to Ithica.
- P.M. Yes, I have all the preceding correspondence. You can get copies of that.

 I remember just as we were starting, and still in Boston our trip almost ended. We were on a divided highway going out of town when the car in front of us suddenly decided to make a "U" turn. It slowed down unexpectedly. I put on the brakes hard throwing us up onto the curb we missed them by a hair. Our car was an oldsmobile as I recall. It would have been a bad accident, and I wouldn't have gotten to see Papez. That certainly would have changed things.

K.E.L. - Did you meet Papez first in the Lab?

P.M. Yes, we went straight to the school and talked about the things we would like to see. He had a number of comparative brain series but it was mostly the Macaque. We were there about $2\frac{1}{2}$ days I guess, and went through the whole brain. It was like walking through a great park with Papez. It was just a lot of fun. My brain was like a sponge - just sopping it up. I learned more anatomy in those few days than in all the rest of my life. Papez gave a continuous running discourse. He would keep seeing these tracts that he 'had always wondered about' and would stop and talk about them. In addition we looked at some gross specimenshuman and subhuman stuff. It must have been with the human brain gross material that he began to point out these other fibers that might be coming in from visual, auditory, and other sensory areas. That was when I got so excited. This was the only thing I could have added to what he had said in 1937 - that there were other possibilities for information getting into the hippocampal formations. That was all I added in the way of anatomical ideas in my 1949 paper.

- K.E.L. What about your later paper on memory the stream of interoceptive information coming in through the hypothalamus and septum going to the basal dendrites of the hippocampal pyramids, while the exteroceptive information goes to the apical dendrites of these neurones?
- P.M. Well, that may not be so crazy. You know I am puzzled to this day about the cingulate gyrus. When we started doing unit recording I thought that the cingulate would light up with visual, auditory and all these other stimuli, but the only thing that showed up was the vagus. I think it must be rather parallel to the hippocampus when you get this sort of unconditional message coming in and then you add the other exteroceptive things to make the whole picture. We never did get any intracellular stuff from the cingulate, but someone will do that.

- K.E.L. Well the end point of that paper you gave me the other night was that the posterior portion of the cingulate - area 23 has primarily sensory connectivity while the anterior area - 24 is primarily downstream motor in its connections - it talks particularly to the striatum.
- K.E.L. Did you talk with Papez about the 1937 paper specifically?
- P.M. Oh, yes we talked a lot about it. He enlarged to me at some length how he happened to write it. He said he had read this announcement from an English foundation I forget which one it was offering a grant of \$150,000 for investigating the mechanisms of emotion. Papez said it made him mad those were his words. The only time when I was there that his language seemed to get a little rough. As much as to say, though he wouldn't, use the expression those bastards offering this grant when we know a lot about these mechanisms already. He implied that he dashed this thing off quickly. That was one thing that Lester Aaronson explained to me later that Paper of Papez was not at all sudden. He had been interested in that problem for years and had been thinking about it and wrestling with it.
- K.E.L. Yes, in some of Papez correspondence with Vonderahe he said that it would be great if we could establish the anatomical mechanisms of emotion as historically emotion had been treated as magic.
- P.M. I think Dart (Raymond Dart) may have been a little put out at Papez because he never referred to a paper put out by Dart in 1935 on the whole structure of the neopallium its history and significance. In that paper Dart made the pitch that the parahippocampal neopallium (he calls it neopallium it should have been the parahippocampal gyrus) controlls the muscular display of emotion. Striatal history offers us a clue as to the divergent activities of the two divisions of the mammalian neopallium. Dart's paper recognizes the pre-pyriform area and the parahippocampal area which are forward in the dorsal convexity of the reptilian brain.

And of course having been a student of Elliott Smith Dart would regard only the pyriform area and the hippocampal formation as paleopallium or I should say old pallium. Elliott Smith in a paper on the natural subdivision of the pallium introduced the word neopallium Pallium was introduced apparently by Reichert in 1859. Elliott Smith takes off from Turner's paper of 1890 in which Turner mentions the rhinal and hippocampal fissures as the dividing line between the old and the new pallium. He felt that the old pallium corresponds to Schwalbe's falciform lobe which would take in the hippocampal rudiment, the indusium griseum, the hippocampal formation and the pyriform lobe. The globus hippocampi is the way Turner referred to it.

- K.E.L. What does globus hippocampi mean?
- P.M. Well there are many definitions. According to Elliott Smith it meant the pyriform temporal lobe so the old Pallium for both Smith and Dart applied only to the falciform lobe of Schwalbe. The cingulate gyrus was neopallium. I discovered today that most people regard the cingulate gyrus as neopallium and don't go along with Paul Yakovlev's designation as transitional cortex or meso-cortex.
- K.E.L. Tell me again what Papez said about the 1937 opus.
- P.M. He said he was mad about this advertisment from England, asking for someone to study this "neglected" area of the neural substrate of emotion. It would be interesting to look up and see if we could find that ad. Anyway he said it made him mad and provided the steam to dash the thing off. But as I said already Aaronson said the emotion paper wasn't dashed off at all he had been worrying about that problem for years in the early 30's when Aaronson was there with Papez.
- K.E.L. Did Aaronson say why Papez never referred to that paper in his subsequent writings?

- P.M. No he never said anything about that. He must have had some strange feeling about it that you were showing a soft side talking about emotion not being a really hard scientist. But he didn't show any of that feeling while we were there. He knew I had come up because of that paper so I suspect he may have been rather glad to talk to somebody who was really interested in the thing. I didn't have any hesitation in talking about it, so he could enjoy it and feel guiltless at least while I was there. He was very animated. I suspect he may not have been so animated, all the time anyway. I think his relations with the outer world were not very joyful and cordial. He may have been rather self-contained. I think like a lot of people who work on the brain, he sort of felt sorry for the rest of the world because of its sheer ignorance and lack of curiosity about the brain.
- K.E.L. How did he react to your paper when it came out in "Psychosomatic Medicine"? Did you have a letter from him about that?
- P.M. Yes I think so.
- K.E.L. Did you send him proofs or anything beforehand?
- P.M. No I don't think so I checked things with him to be sure I wasn't misquoting him. He was very gracious and generous and said he was pleased with my 1949 article.
- K.E.L. That was quite a show having Papez take you through the entire brain of the Macaque.
- P.M. Yes, take for example Muratoff's bundle. How many people worry about a topic like that? About Muratoff's bundle the ancient commissures, the subcallosal bundle, the supraoptic etc. We spent quite a bit of time discussing those tracts and their possible origins and where they were going. We went into quite a bit of depth about those things you don't have time to do that often, anywhere. It was quite a remarkable experience.

We had had this correspondence beforehand. He picked the times. It must have been a time when he had a let up in teaching. I don't recall having any students around. I think it must have been the Easter holidays. He just took time off from his usual routines and devoted himself to talking about these questions. We did go over to his house one evening and had an interesting time there, too.

- K.E.L. You brought Papez back to the attention of the Neuroscience world.
 That was very important.
- P.M. Actually it is rather shameful if that is the case.
- K.E.L. It is a shame on the rest of the world not on Papez or on you. What I can't account for is why he left that important paper and subject lying fallow?
- P.M. That question is hard to answer. The reason was not apparent in any of my contacts with him. He came to visit us later in New Haven. He was there for New Years in 1950. Allison remembers that visit and enjoyed both Papez and his wife Pearl.

We talked then about Paul's laboratory and about his retirement which will come shortly. He is now 67 and will continue working until he is 70.

P.M. - This kind of laboratory will have to survive one way or another, someplace. What other places in the country have the kind of convergence and symbiosis that we have here? I don't think there are any, do you?

There really aren't any in Europe either. It is terrible. They don't have the brain side going - Sieweesen for example is behavior altogether - Konrad Lorenz and his people.

So, a lot of people made model airplanes before they got one up that could fly. You can see the direction things are going. The world has to get into the brain, though there is the potential there of having

too much knowledge. When you look at history which is pretty short, and begin to throw in this limbic business, and realize that limbic is a reality. For better or for worse it is not the brain of reading, writing, and arithmetic. The limbic brain has a different code, and the exchange has to be on a different level. People might begin to realize that our universe and everything in it is up here - in our noggin. This is not to deny the world out there - but time and space is not out there - it is up here in our heads.

I don't think the world wants necessarily to get this message all of a sudden. I think there are ways to come at it and indirectly. Certainly you can do it through epilepsy as we have been discussing. If you use epilepsy as Hughlings Jackson was doing - as a display of brain function.

There is a final rambling discussion - Carl Sagan and his construction of the world. Ursula Franklin and the "male" orientation to the world - to maximize gain (i.e. exploit) vs. the female orientation to minimize disater (i.e. to conserve) and the A.A.A.S. Symposium "Canada as a Conserver Society" (January, 1981). Further discussion included the Iranian Revolution "which makes an awful lot of sense" as a protest against exploitation/depletion - the brain is bright enough to know that, etc.