In accordance with our discussion on Saturday, I propose that your principal job this summer be the construction of an apparatus for making heat capacity measurements.

In addition, I suggest that you start some experiments on oxygen utilization by brain tissue, resembling those carried out by McIlwain.

Mr. John Clauser, the young man from Maryland about whom I talked with you, will arrive in Pasadena on 17 June, and will come to the laboratory on 20 June. I have asked him to come to see Mrs. Harris, who will turn him over to you. He is to start work on that day. Mrs. Harris might have him fill out the employment form. He is to work full time—a forty-hour week—and to receive the standard stipend given to freshmen students in the California Institute of Technology. He will become a freshman student in October. He is interested in electronics, and should be a useful assistant to you.

Professor Albert Tyler in the Biology Division has offered to lend us some apparatus for use in the respiration experiments. The apparatus that he will lend us includes a water bath, a shaker, and half dozen Warburg tubes. You will probably have to make some special Warburg tubes for the experiments involving an electric current, in order that the electrodes can be attached. These tubes can be made to fit onto the regular Warburg manometers. You might want to talk with Professor Tyler before I get back, 23 June. He can tell you something about the operation of the apparatus. You may have made use of this technique already at some time.

I suggest that a repetition of one or two of McIlwain's experiments be carried out, with metallic electrodes (silver or gold plated platinum), in order to see if you can check his curves. Then the same thing should be done with calomel electrodes. You can find in one of the volumes of techniques of physical chemistry how calomel electrodes are made. The calomel is made by precipitation of mercurous ion with chloride ion, followed by thorough washing.

I am interested in the question of how an electric current could increase respiration of brain tissue. I think that a reasonable possibility is that the respiration rate is determined by the concentration of some substances in the tissue, which may become exhausted, and that these substances have electric charges, so that the electric current pulls them from the region of the solution where they are not being used up into the place where they are being used up, thus increasing their effective concentration.

You may remember that I mentioned the other day that the anticonvulsants such as trimethadione might be operating in part at least by changing the electrode potential of the electrodes. It might be worth while to check on this by a simple experiment, consisting in putting silver electrodes in a solution of sodium chloride, measuring the current as a function of applied voltage, at, say, 60 cycles, and then repeating the experiment with trimethadione present in the solution. In each case the relation between current and applied voltage should be a curve with a
foot at somewhere around one or two volts. The trimethadione might shift the foot by changing the overvoltage at the electrodes. This is an experiment that does not involve brain tissue at all. If McIlwain had made his setup in such a way that he recorded the current flowing as well as the applied potential difference between the electrodes, he could have learned much more than he did.

The operation of the Warburg apparatus requires some care, and it is time consuming to carry out a large number of experiments. I suggest that your plan for the summer be to get a series of experiments along these lines set up, for Mr. Clauser to carry out when he doesn’t have other jobs to do, but that you use him to the maximum extent possible in connection with the construction of the heat capacity apparatus, and put him on the Warburg studies only when he is not needed for the other job.

Dictated by Professor Pauling
Signed in his absence: Jh

P.S. In carrying out the Warburg studies, I think that you would find it worth while to measure the current as a function of applied voltage for a sodium chloride solution, first with metallic electrodes and then with calomel electrodes. For calomel electrodes, of course, the current would simply be proportional to the applied voltage. With metallic electrodes there would be a foot on the curve, followed by a linear section. If you add trimethadione or other substances to the sodium chloride, no effect of the added substances should be found on the conductivity with calomel electrodes, but a change in the foot might be observed with metallic electrodes. This may be the explanation of McIlwain’s observations.

Dr. Shaw has suggested that in your work on brain tissue it would be worth while to compare the effect of trimethadione with that of other substances that are related to it in chemical structure, such as creatinine. You might want to ask Dr. Shaw for his recommendations, when you reach that point in the experimental work.

Also, Dr. Shaw has suggested that you should compare liver slices with brain slices. I think it might be worth while to check up on the effect on respiration of a bacterial culture, such as E. coli. We should track down the mechanism of the phenomenon of the effect of an alternating current on respiration of tissue slices.

L.P.