THE RELATIONSHIP BETWEEN THE BIO-ELECTRIC POTENTIAL OF RATS AND CERTAIN DRUGS*

H. S. BURR AND PAUL K. SMITH

One of the problems which arises in connection with the study of relatively steady state bio-electric potentials in the living organism is that of the relationship between potential gradients and chemical processes. It has been shown in a number of publications that menstruation (Burr and Musselman[3]), ovulation (Burr, Musselman, et al.[4]), growth (Burr and Hovland [1,2]), and cancer (Burr, Strong, and Smith[5]) all produce changes in the bio-electric properties of the organism. On the other hand, Meader and Marshall[7, 8] have shown that wide changes in the body temperature in mice produce no consistent alteration in the potential gradients. Dusser de Barenne, McCulloch, and Nims[6] found no consistent correlation between pH and the DC potential of the cerebral cortex in monkeys.

As a control for the above experiments, it seemed worth while to determine whether or not anesthetics or a number of other drugs of wide systemic action would produce any effect measurable in terms of bio-electric properties. So far, all of the significant correlations were found in connection with activities which presumably are located in or are confined to a particular part of the whole organism. Ovulation, presumably, is a local phenomenon, so also are cancer and wound healing, and differential growth rates are known to exist in the embryo. While all of these may have some general effect, nevertheless, they can be considered in all probability local differences. The drugs chosen, while exhibiting specificity for certain tissues, undoubtedly have a very widespread general effect.

In order, therefore, to eliminate the chemical factor as a significant variable in the determination of over-all body potentials, a series of experiments was carried out on white rats to which were administered a variety of drugs. The technic was relatively simple. The rats were confined in a suitable animal-holder and the chest, sternum, and symphysis were shaved. Glass tubes connected with the silver-silver chloride electrode chambers were then placed on

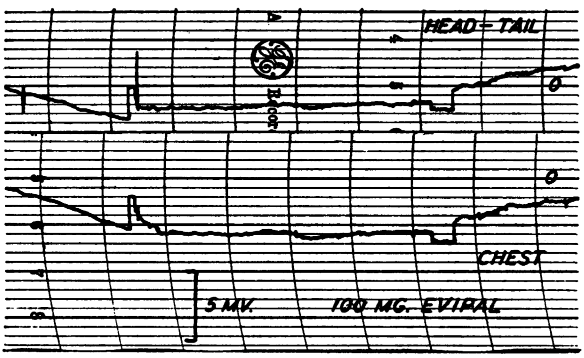
* From the Departments of Neuro-Anatomy and of Pharmacology and Toxicology, Yale University School of Medicine.

the body and the silver-silver chloride electrodes connected with the Burr-Lane-Nims microvoltmeter. Continuous records of the changing potential gradient were made by means of a General Electric photo-electric recorder. After a short run of a few minutes to determine the base body potential, the drug under test (except for ether) was administered by intraperitoneal injection and the recording continued for a sufficient length of time to cover any probable change. The drugs used included depressants and excitants of the nervous system and certain peripherally acting agents. In all, 59 animals were used, in the majority of which simultaneous determinations were made across the chest and between the xyphoid and symphysis. Eight of the animals served as normal controls. In each instance the mean of all the determinations was taken and standard deviation computed. The significance ratio was determined if the number of cases warranted. The dosage employed in each case is indicated in the table, except in the case of ether. It will be noted that sodium amytal and seconal, particularly the latter, seem to decrease slightly the potential gradients across the chest and between the xyphoid and

	No.	*Chest-chest*			*Head-tail*		
	animals	*mean*	*SD*	*SR*	*mean*	*SD*	*SR*
Normal controls	8	4.6	3.6	....	3.7	2.6	....
Ether	3	5.8	....	....	2.7	....	....
Sodium amytal, 90 mgm./kgm.	9	3.0	2.8	1.7	6.0	6.6	1.4
Seconal, 50 mgm./kgm.	4	1.8	0.9	3.6	1.7	1.5	2.6
Evipal, 100 mgm./kgm.	4	4.2	2.2	0.4	4.4	....	....
Morphine sulfate, 100 mgm./kgm.	2	2.0	....	....	2.5	....	....
Strychnine sulfate, 5 mgm./kgm.	16	3.6	3.0	1.1	2.4	2.3	1.4
Cocaine hydrochloride, 90 mgm./kgm.	5	2.8	0.9	2.3	....	....	....
Epinephrine hydrochloride, 2 mgm./kgm.	3	2.8	1.0	....	....	....	....
B-methyl-acetyl-choline bromide, 100 mgm./kgm.	3	2.0	....	....	....	....	....
Histamine phosphate, 3 mgm./kgm.	2	3.2	....	....	....	....	....

symphysis. On the other hand, strychnine, which produced profound physiological disturbances, had virtually no effect. Cocaine possibly produced a very slight change but the significance is doubtful. Epinephrine, histamine, morphine, and acetyl-choline gave no consistent alteration. There seems to be a slight tendency for the administration of ether to raise the potentials across the chest, but the significance of that elevation is doubtful.

It seems clear, under the conditions of the experiment, that the administration of the above-mentioned drugs produces little or no effect upon the potential gradients. At least, such changes as may be present are either not of the order of magnitude to be found in those cases where significant correlations can be seen or else do not appear on the surface of the organism. Changes in potential which may be associated with growth, ovulation, carcinogenesis, etc. involve many millivolts, but the differences here recorded are in the order of microvolts. In all probability, so many variables exist in the system that a change in any one of them must be of considerable magnitude to produce a general or over-all effect.



Simultaneous, continuous, photo-electric records of potential gradients in the white rat. The upper record is of the head-tail gradient between the xyphoid and symphysis, and the lower record is of the gradient across the chest. Both immediately follow the administration of 100 mgm./kgm. of Evipal. The similarity of the two curves is striking.

It will be noted that in approximately half of the animals simultaneous determinations were made, using four points of contact and two recording instruments. If one compares these simultaneous records one finds a rather extraordinary parallelism in the changing potentials. Even minor changes in the head-tail gradient have their counterpart in the cross-chest gradient. This lends further support to the idea that these potential gradients are not chaotic, but rather are organized into a systematic pattern as has been recorded in numerous other determinations (Northrop and Burr[9]).

The above data present little evidence of any profound effect of the administration of the drugs investigated on the bio-electric potentials recorded in the white rat.

References

1 Burr, H. S., and Hovland, C. I.: Bio-electric potential gradients in the chick. Yale J. Biol. & Med., 1937, *9*, 247.

2 Burr, H. S., and Hovland, C. I.: Bio-electric correlates of development in Amblystoma. Yale J. Biol. & Med., 1937, *9*, 541.

3 Burr, H. S., and Musselman, L. K.: Bio-electric correlates of the menstrual cycle in women. Am. J. Obst. & Gynec., 1938, *35*, 743.

4 Burr, H. S., Musselman, L. K., Barton, D., and Kelly, N. B.: Bio-electric correlates of human ovulation. Yale J. Biol. & Med., 1937, *10*, 155.

5 Burr, H. S., Strong, L. C., and Smith, G. M.: Bio-electric correlates of methylcolanthrene-induced tumors in mice. Yale J. Biol. & Med., 1938, *10*, 539.

6 Dusser de Barenne, J. G., McCulloch, W. S., and Nims, L. F.: Functional activity and pH of the cerebral cortex. J. Cell. & Comp. Physiol., 1937, *10*, 277.

7 Marshall, C., and Meader, R. G.: Studies on the electrical potentials of living organisms. I. Base-lines and strain differences in mice. Yale J. Biol. & Med., 1937, *10*, 65.

8 Meader, R. G., and Marshall, C.: Studies on the electrical potentials of living organisms. II. Effects of low temperatures on normal unanesthetized mice. Yale J. Biol. & Med., 1938, *10*, 365.

9 Northrop, F. S. C., and Burr, H. S.: Experimental findings concerning the electrodynamic theory of life and an analysis of their physical meaning. Growth, 1937, *1*, 78.