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Action of Pentamethylenetetrazol (Metrazol) and Insulin on Brain Potentials of the Rabbit.

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The use of pentamethylene tetrazol (metrazol) and insulin shock therapy in schizophrenia has prompted several investigations in this laboratory upon the actions of these agents given in convulsive doses. This report deals with some of these actions upon the potentials recorded from the intact rabbit cortex.

Recordings have been made with electrodes of the type described by Rheinberger and Jasper[1] placed symmetrically on the precentral and striate areas of the rabbit. Potentials were led through condenser coupled amplifiers to moving coil oscillographs. Other records were made with paired silver tube electrodes (Adrian)[2] following trephination. Curare and artificial respiration have been

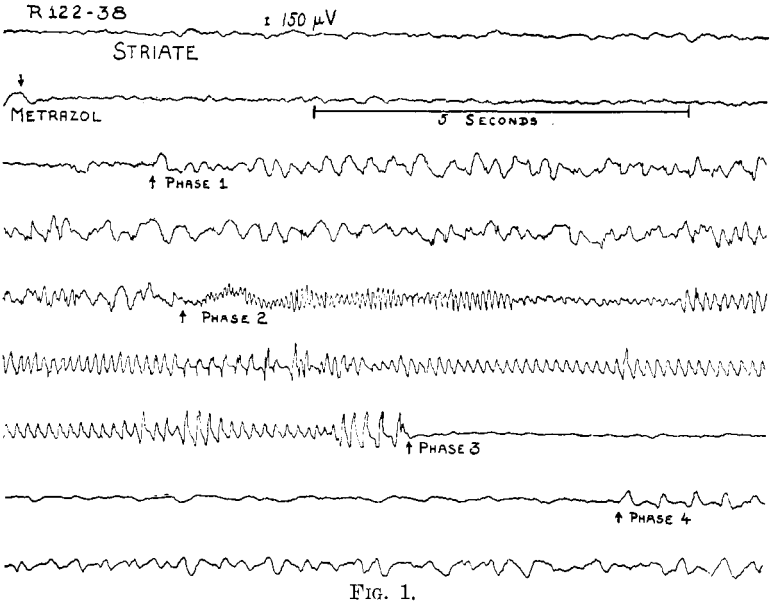

Fig. 1.

[1] Rheinberger, M. B., and Jasper, H. H., *Am. J. Physiol.*, 1937, **119**, 186.
[2] Adrian, E. D., *J. Physiol.*, 1937, **88**, 127.

used in experiments with metrazol to obviate the gross movement artefacts, but with insulin, the use of curare has been found impractical, due to its hyperglycemic action, which prevented the occurrence of convulsions in all our earlier experiments.

Metrazol. Fig. 1 shows a continuous record of the average metrazol convulsions, the potentials being recorded with paired leads on the area striata. There are 4 clearly defined phases following the latent period, which varies from 3-12 seconds. Phase 1 lasts from 2-21 seconds in primary convulsions and has a wave form very close to that recorded in human petit mal epilepsy. This phase is usually absent in the later secondary convulsions which often occur. Phase 2 lasts from 23-75 seconds, phase 3 from 0-13 seconds, while phase 4 is prolonged, lasting for one hour and up.

The first and second phases are probably due to the direct action of the metrazol. The third phase is possibly a true post-activity depression. The fourth phase may be due to the diminished blood flow noted by Leibel and Hall[3] with a resultant impairment of cortical function. No exact correlation with motor phenomena has as yet been possible due to the necessity for using curare.

Insulin. Fig. 2 shows representative excerpts from a record obtained with bilateral leads on the precentral and striate regions. There is a progressive increase in slow wave activity during the preconvulsive stage. Following convulsion the slow random type of wave continues for some time. Glucose, given in either the preconvulsive or postconvulsive stage, will interrupt the slow wave production, substituting a more normal type of activity. Imme-

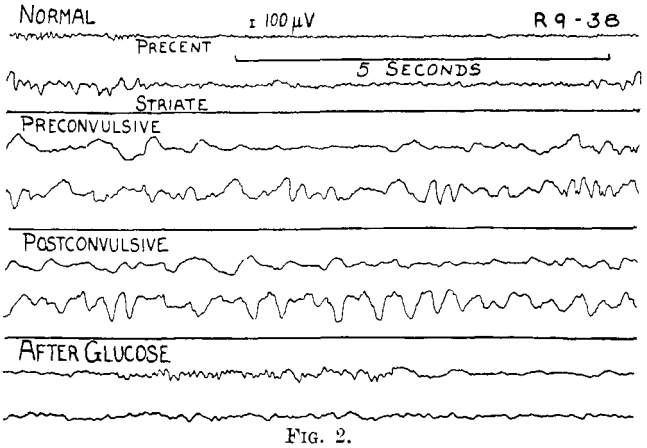

FIG. 2.

[3] Leibel, B. S., and Hall, G. E., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 894.

diately following a convulsion there may be a period of post-activity depression as in the case of the metrazol experiments.

A prolonged course of injections of insulin or metrazol in convulsive doses, (30-36 injections over 58-63 days) has not appreciably altered the course of the convulsive response from that observed in previously untreated animals.

The most conspicuous similarity between the actions of metrazol and insulin on cortical potentials is the prolonged phase of random slow wave production, which may possibly be correlated with the period of reduced cerebal blood flow[3] and coma.

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Lead Analyses of Hair as an Indication of Exposure to Lead.

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Meillère[1] believed that the hair acts as a channel of lead excretion from the body. The implications of this finding, if correct, in relation to medical and industrial problems involving serious exposure to lead are obvious. Inasmuch as Meillère made no attempt to determine the extent of contamination of his material, his thesis requires further support before it can be accepted. Previous work in this laboratory[2] has confirmed that of numerous investigators indicating that lead is extremely widespread. It is obvious, therefore, that before this question of true lead content of hair can be studied properly, it is necessary first of all to obtain a complete removal of that which is present as an external contaminant. Experiments were performed for the purpose of revealing how such contaminating lead may be removed. For example, after treatment with ether to remove lipoidal material, hair was washed in soap solution, and then in acetic and nitric acids with the idea that the lead could be removed as the soluble salts, but this technic gave unsatisfactory results. Finally, trials were made of the efficacy of treatment with diphenylthiocarbarzone in chloroform, the reagent found so useful in analysis for lead. When lead in known amounts

[1] Meillère, M. G., *Compt. rend. Soc. de biol.*, 1902, **54**, 1134.

[2] Horwitt, M. K., and Cowgill, G. R., *J. Pharm. Exp. Ther.*, 1937, **61**, 300.