

### 136. Inhibitory Action of Carcinostatic Substances introduced into C.S.F. of Dogs upon Electroshock Seizure Threshold

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Intrathecal application of  $\gamma$ -amino  $\beta$ -hydroxybutyric acid (GABOB) with Homocarnosine (HC) to epileptic patients cured completely the attacks by the observations for 3.5 years. It must be presumed that GABOB or its derivatives had an action upon DNA or RNA, which were involved in enzymes which produced excitatory substance.

The author tried to apply carcinostatic substances into c.s.f. of dogs several times every other day, to produce a dog of which the threshold of electroshock seizure should be reduced. And the following results were obtained;

- 1) 0.1 mg of Nitrogen mustard N-oxide was applied intrathecally every other day. After 8 days it showed a) strong inhibition on electroshock seizure threshold and it lasted for 12 days, b) shortening of seizure duration by same stimulus.
- 2) Inhibitory effective dose of Nitrogen mustard N-oxide were between 0.25 mg-0.1 mg.
- 3) For 8-azaguanine, it was 3.5 mg-7 mg.
- 4) Hg-hematoporphyrin Na and Mitomycin C had only slight inhibition.
- 5) Chromomycin A<sub>3</sub> had no inhibition.

### 137. Metabolism of Homocarnosine and Inhibitory Effect of Homocarnosine on the Seizure induced by Citrate-Na

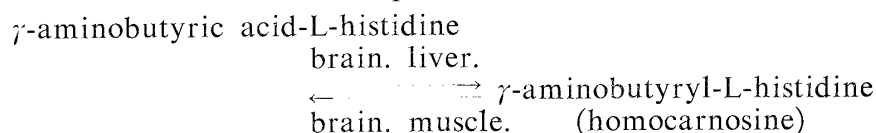
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Homocarnosine ( $\gamma$ -aminobutyryl-L-histidine) has been isolated from beef brain in amounts of about 0.5 to 1 mg/100 g tissue by Pisano et al (1960).

Mori et al (1963) reported that homocarnosine is an inhibitory transmitter of the CNS of ep-mouse. The present report is a result of the studies on the metabolic pathway of homocarnosine and on the anticonvulsive effect upon the convulsive fit induced by the cystemally administrated citrate-Na.

1) Metabolism of homocarnosine:  $^{14}\text{C}$ -labeled GABA or homocarnosine was incubated with slices of mouse organs in vitro and metabolic products of these substances in these organs were investigated by using with tracer method. The results of these experiments were as follows;



2) Anti-convulsive action against the convulsive fit induced by citrate-Na: A clonic convulsion was observed, when 2 mg/kg of citrate-Na was administered to the cisterna magna of rabbit. On the contrary, no convulsive fit was observed in the case of administration of 5 mg/kg of homocarnosine before administration of convulsive dosage, no convulsion was occurred. These experimental results show that homocarnosine is an effective anticonvulsant for the convulsion induced by citrate-Na. This fact was also clarified by the EEG studies simultaneously.

### 138. Epileptic Fits Producing Effect of Carcinogenic Substances applied to the Brain via C.S.F. of Dogs

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Karahashi, and Yagishita reported that the carcinostatic substances by intrathecal application to the central nervous system, reduced continuously the electroshock seizure threshold of dogs.

We tried to make epileptic dogs by an intrathecal continued application of carcinogenic substances, and obtained the results as follows.

1) Application of  $\beta$ -naphthylamin, *p*-dimethylaminoazobenzene, 20-methylchorantren, and 4-nitroquinolin *N*-oxide, only did not produce convulsive dogs.

2) 2 mg of 20-methylchorantren with 0.2 mg of methionine sulfoximine were applied. Seizures were observed with 15–20 hours latent period. At first, it appeared every 5–10 min. continuously and after 52 hours approximately abolished. Some of them died, but others were alive. In the latter cases the frequency of their seizures decreased during 3 or 4 days, and finally it ceased.

3) Methionine sulfoximine alone was seizure producing over 0.5 mg application, but in the above experiments they were all under the critical