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Effect of γ-aminobutyric acid upon brucine convulsions

SIR,—γ-aminobutyric acid (GABA) when applied to the surface of the cerebral cortex of certain mammalian species has been shown to protect the animals from electrically or chemically induced seizures (Purpura & Grundfest, 1956; Purpura, Girado & Grundfest, 1957). Furthermore it has been shown by several investigators that acute parenteral administration of GABA protects animals from electrically or chemically induced seizures (Hawkins & Sarett, 1957; McLennan, 1957; 1958). During the course of our experiments we found that, shortly after parenteral administration of GABA (3·0 g/kg) to rats, no protection from electrically induced seizures and strychnine seizures was observed. Pylkkö & Woodbury (1959) showed that the CD50 of strychnine was increased in rats pretreated with GABA 72 hr before treatment with the convulsant.

Since brucine differs from strychnine by having two methoxyl groups attached to the aromatic ring, it was of interest to study the possible protective properties of GABA against brucine seizures and to study the time course of any protective properties found.

Mature male albino Holtzman rats were pretreated with 3·0 g/kg GABA intraperitoneally and brucine alkaloid was administered after 3, 8, 15, and 30 days. The CD50 values for these animals were calculated ($CD50_1$) according to the method of Litchfield & Wilcoxon (1949). The CD50 values for brucine alkaloid ($CD50_2$) were calculated at the same time intervals for rats without GABA pretreatment. The potency ratio (P.R. = $CD50_1/CD50_2$ and the $f_{P.R.}$ were calculated by the method of Litchfield & Wilcoxon (1949).

TABLE 1. EFFECT OF GABA ON CD50 OF BRUCINE ON GROUPS OF 36 RATS

Weight of rats g	Days after GABA	$CD50_1$ with GABA	$CD50_2$ without GABA	Potency ratio	$f_{P.R.}$
83–132	3	117·0 (92·1–148·6)	71·8 (61·0–83·3)	1·63 (1·20–2·20)	1·35
112–170	8	91·0 (70–118·3)	69·8 (61·2–79·6)	1·30 (0·96–1·75)	1·35
112–218	15	88·0 (69·3°111·7)	72·0 (61·5–84·2)	1·22 (0·9–1·65)	1·35
93–220	30	82·0 (74·6–90·2)	82·0 (73·2–91·0)	1·0 (0·83–1·20)	1·2

It is evident from Table 1 that three days after GABA administration, the CD50 of brucine was elevated significantly. Thus the present observations seem to indicate that the anticonvulsant activity of GABA is not seen until three days after its parenteral administration.

Since Eccles (1956) has established that strychnine selectively blocks the inhibitory synapses in the central nervous system, it is possible that its dimethoxyl derivative, brucine, acts similarly. It is therefore of interest that the convulsant

activity of brucine is altered three days after a single dose of GABA, but whether GABA or a metabolite is responsible for this effect remains to be determined.

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Anti-anaphylactic action of water-soluble glucocorticoids

SIR,—Natural and synthetic glucocorticoids have proved to be highly active in clinical practice for the treatment of various allergic conditions and the prevention of surgical shock. But in animal experiments most authors have shown steroid treatment to be ineffective in experimental anaphylactic shock (Herxheimer & Rosa, 1952; Goadby & Smith, 1964).

We have now compared, using the intravenous route, a new water-soluble steroid Depersolon (11,17-dihydroxy-21-(4-methylpiperazin-l-yl)-pregna-1,4-diene-3,20-dione hydrochloride) (Tóth, Tuba & Szporny, 1961; Görög & Szporny, 1963) with the water-soluble prednisolone sodium hemisuccinate and dexamethasone-21-phosphate for their capacity to confer protection on guinea-pigs in shock induced by an albumin aerosol.

Anaphylactic shock was produced by the micro-shock method of Herxheimer (1952). Guinea-pigs of 250–400 g were sensitised with 5% commercial crystalline albumin solution, 75 mg per animal, injected intraperitoneally. After three weeks the animals were placed in a plastic box and 5% egg albumin aerosol was introdced into the chamber The point when the animal exhibited signs of severe dyspnoea, lying down on its side and turning its head to right and left, was taken as the preconvulsion time. If aerosol treatment is discontinued at this juncture, the animals can be saved from certain death by oxygen insufflation as recommended by Smith (1961).

Preconvulsion time was assessed initially on the 21st day after sensitisation and then twice more at weekly intervals. The average of the two latter values was taken as control. On the fourth occasion the drug was injected into the jugular vein of unanaesthetised guinea-pigs at various times before giving the albumin aerosol. The control group was given physiological saline under similar conditions.

The measure of protection was represented by the quotient of post-treatment and control preconvulsion times (Ratio = R). Protection was considered as maximal when R was 10.

The findings in Table 1 show that the new steroid exerted a strong protective influence against anaphylactic shock, the effect reaching a peak 10 min after