validity of these conclusions is supported by the fact that the preparations of hormones used in these experiments were shown to be physiologically active at the dosages used. This finding substantiates the work of CAVANAGH and JOSEPH[17] and challenges the accepted ideas about the mode of action of ACTH in promoting regrowth of axons[13,14]; strongly suggesting that an alternative explanation for the ability of these substances to induce regeneration must be sought.

FERTIG et al[1] showed that both T3 and ACTH can promote regeneration in the mammalian CNS. However it was not possible to demonstrate regeneration in the present experiments simply because the leakage of CSF from the ventricle into the incision produced a cavity which could not be bridged by axons.

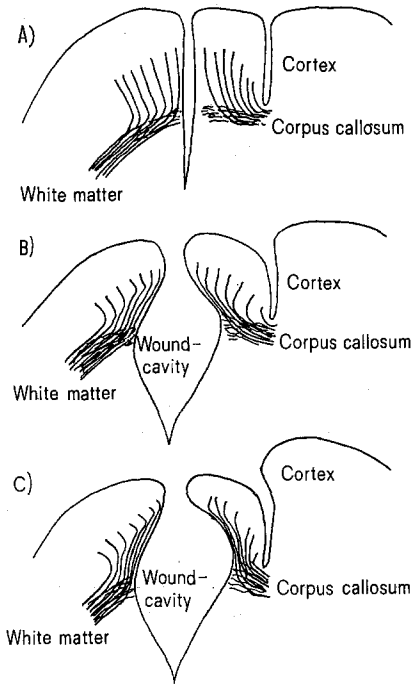

Fig. 3. Proposed explanation through A to C. for the formation of the tract of axons seen to lie along the edges of the wound in animals sacrificed 50 and 100 days after operation.

Résumé. Une étude quantitative des effets de ACTH et T3 sur la réaction des cellules gliales dans le corpus callosum, après incision, a montré que ces 2 hormones n'ont aucun effet sur cette réaction. Ainsi, on ne peut plus soutenir l'idée généralement acceptée que ces hormones provoquent une régénération partielle de l'axone central du système nerveux, en modifiant la cicatrice gliale.

G. FLINT and M. BERRY[18]

Department of Anatomy, The Medical School, University of Birmingham, Birmingham B15 2TJ (England), 13 September 1972.

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[18] Acknowledgments. The authors are indebted to Mr. R. MORRIS at the Women's Hospital, Birmingham, for the assay of corticosterone and to Mrs. S. BUCKLEY for preparing the many slides for histological examination.

Iproniazid Interaction with the H^3Norepinephrine Uptake and Retention, on Isolated Left Atrium of Guinea-Pig

In a early paper from our laboratory, iproniazid (IPN) was found to be a blocking agent of the H^3norepinephrine (H^3NE) uptake by isolated ventricle of frog[1]. However, it was desirable to elucidate if this blockade was produced at the neuronal membrane ($uptake_1$) or intraneuronally, namely, by diminishing the re-entry of H^3NE into the storage vesicles present in sympathetic nerve endings.

In other studies on isolated atria of guinea-pig (unpublished results), we observed that the increase of H^3NE uptake between reserpinized atria, treated with IPN, with respect to their controls without the MAO inhibitor, was very much higher than the increase of the H^3NE uptake observed in no-reserpinized atria, treated with IPN and their untreated controls. These observations are in agreement with those reported by other investigators[2]. The facts prompted us to think that IPN blocked the re-entry of H^3NE into storage vesicles, so that this blockade was only present in unreserpinized atria, diminishing the difference in the incorporation of H^3NE between the atria treated with IPN and their untreated controls.

If we accept this hypothesis the treatment with IPN could produce a disturbance in the turnover of NE at the sympathetic nerve endings, by diminishing the inflow and by maintaining unchanged the outflow. Consequently, the normal rate of NE from the storage vesicles will decrease. In the present paper, it has been studied whether IPN blocks the incorporation of H^3NE into storage vesicles present in the nerve endings of the isolated atrium of the guinea-pig.

Methods. The experiments were carried out with guinea-pigs of either sex weighing from 500 to 800 g. The left atrium was isolated and mounted as previously described by FURCHGOTT et al.[3]. In each experiment one half of the atrium served as a control and the other half as the experimental preparation. The Krebs-bicarbonate solution used contained 10^{-5} g/ml of ethylene diamine tetraacetic acid (EDTA) and 10 m*M* of glucose through which 95% O_2 and 5% CO_2 or 95% N_2 and 5% CO_2 was continuously bubbled. Each half was subjected to a resting tension of 1 g and was electrically driven at a rate of 30 beats/min. Atria were attached to force displacement transducer (Grass, model FT03) and mechanical activity was recorded by a Grass polygraph.

Under their respective conditions, halves were then incubated with 5 ng/ml of d, l-H^3NE (specific activity, 16, 7Ci/mmol, New England Nuclear Corp.) for 5 min and then thoroughly washed. 4 additional washes were given over the subsequent 40 min period at the end of which

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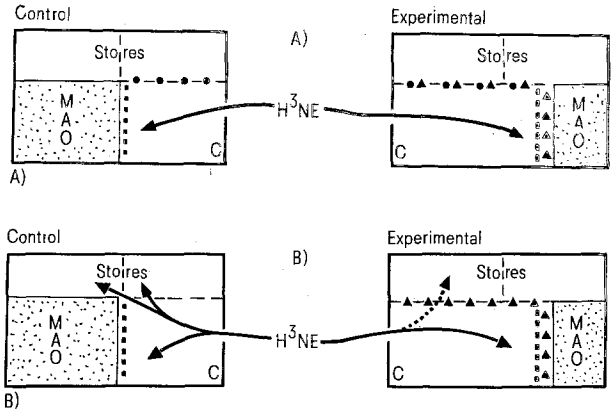
Effect of the MAO inhibition by iproniazid and a nitrogenated medium on the H^3NE uptake in isolated left atrium of guinea-pig

N [a]	Reserpine [b]	Oxygenated medium (min)	Pretreatment (min) [c]	Nitrogenated medium (min) [d]	H^3NE present incubation (5 min)	H^3NE in tissue 45 min after washout (dpm/g) [e]
6	Treated	30	Iproniazid 20	40	5 ng/ml	433.600 ± 31.693
	Treated	30	—	40	5 ng/ml	233.383 ± 70.571
7	—	30	Iproniazid 20	40	5 ng/ml	738.667 ± 91.807
	—	30	—	40	5 ng/ml	1033.070 ± 95.851

[a] Number of experiments (paired); [b] 5 mg/k (18–24 h before); [c] 5.10^{-4} g/ml [d] This medium was present until the end of the experiment; [e] Mean ± S.E.M.

the halves were removed for analysis of radioactivity. All preparations were performed at 37°C. The H^3NE extraction was performed according to the method of ANTON and SAYRE[4] and radioactivity was counted in a Nuclear Chicago Liquid Scintillation Spectrometer, model 725. All samples were corrected for quenching with an automatic external reference standard. Under our working conditions, the radioactivity present in the alumina eluates cannot be ascribed to metabolites of H^3NE but to H^3NE itself[5]. H^3NE is expressed in terms of disintegrations per min/g of tissue (dpm/g). When we refer to H^3NE uptake, we mean H^3NE uptake and retention by isolated atrium of the guinea-pig. The dose of the iproniazid phosphate (Roche) is expressed in terms of g of salt per ml of bath solution. Statistical significance of the difference between means was determined by the *t*-test for paired data.



This figure is proposed in order to explain the results obtained in the present work.●, site of action of the reserpine; ■, site of action of the N_2; ▲, site of action of the iproniazid. Stores, NE storage vesicles (depleted and blocked by reserpine); C, neuronal cytoplasm.

A) Reserpinized preparations treated with N_2. Control: The exogenous H^3NE incorporated and retained into C (since MAO are inhibited by N_2 and the stores are blocked by reserpine) Experimental: Pretreated with IPN. Exogenous H^3NE incorporated and retained into C but in a higher amount than the control, since MAO are strongly inhibited (by IPN + N_2). Stores are blocked by reserpine and probably by IPN. B) Unreserpinized preparations, treated with N_2. Control: Exogenous H^3NE incorporated into C and into the stores. Experimental: Exogenous H^3NE incorporated and retained into C and possibly small amounts into the stores (dependent upon the intensity of the blockade, according to the concentration of the administered iproniazid). It should be noted that there is an increased incorporation in the experimental preparations with iproniazid A) in the reserpinized atria; however in no-reserpinized atria (B), the incorporation is higher in control preparations (no-IPN), as explained by the results shown in the Table.

Results and discussion. In 6 experiments carried out with reserpinized guinea-pigs, both halves of the atrium were bubbled through with a mixture of 95% O_2 and 5% CO_2 (30 min). One half was pretreated with IPN (5.10^{-4} g/ml, 20 min). The other half remained as a control. At the end of this treatment and after washout, the MAO inhibition was produced by displacing the oxygenated Krebs solution with a Krebs solution bubbled through with a gas mixture of 95% N_2 and 5% CO_2, in both preparations[5]. 4 washes were given after a period of 40 min and halves were then incubated with H^3NE. The incubation and the washout was carried out under a atmosphere of N_2.

The Table shows an increased incorporation of H^3NE ($P < 0.02$) with respect to their controls in atria treated with IPN. These results could be explained as follows (Figure, A): In controls, MAO inhibition produced by N_2 would be responsible for the H^3NE retention in the neuronal cytoplasm since the stores would be blocked by reserpine. On the contrary, in experimental halves, the MAO inhibition would be more potent because of the association of both MAO inhibitors (IPN plus N_2), which would produce a enhanced capacity of the cytoplasm to incorporate and retain H^3NE. The stores would also be blocked by reserpine and probably by IPN.

In order to explain the possibility that IPN blocks the incorporation of H^3NE into stores, 7 experiments were carried out under circumstances similar to those of the preceding experiments but with unreserpinized atria. The Table shows a marked decrease in the H^3NE uptake in preparations treated with IPN compared with their corresponding untreated controls ($P < 0.01$).

The paradoxical fact that IPN appears to be a blocking agent of the incorporation of H^3NE in no-reserpinized preparations, can be explained in this way (Figure, B): In controls, H^3NE was incorporated not only in the neuronal cytoplasm by the MAO inhibition (produced by N_2) but also in the storage vesicles, since atria proceded from no-reserpinized animals and the energy necessary for the uptake, retention and re-entry into storage vesicles was not affected by the anoxia[5]. However, in experimental

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preparations (Figure, B), IPN would block the incorporation of the labelled amine in the storage vesicles and the total amount of H^3NE in the tissue would consequently be decreased in comparison with their controls.

The results obtained in the present paper confirm the hypothesis that IPN blocks the incorporation of H^3NE into storage vesicles present in the nerve endings.

Resumen. La incorporación de H^3NE a la auricula aislada de cobayo reserpinizado, tratado con Iproniazida (IPN) y atmosfera de Nitrogeno, es superior a la de sus controles sin IPN. En auriculas no reserpinizadas, la IPN aparece como agente bloqueante de la incorporación. Se sugiere que este bloqueo ocurre a nivel de las vesiculas especificas de almacenamiento presentes en las terminaciones nerviosas adrenergicas.

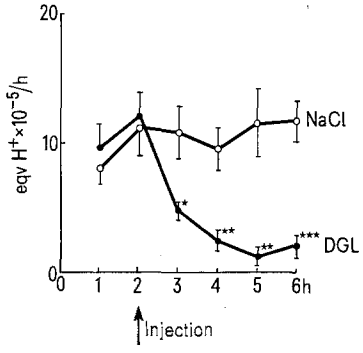
R. MARTINEZ-SIERRA, A. VELASCO-MARTIN and P. D. GARCIA DE JALON

Departamento de Farmacologia, Facultad de Medicina, Ciudad Universitaria, Madrid 3 (Spain),
24 November 1972.

Effect of Deglycyrrhizinized Liquorice on Gastric Acid Secretion, Histidine Decarboxylase Activity and Serum Gastrin Level in the Rat

Liquorice has been claimed to promote the healing of gastric ulcers in man. However, serious side effects such as water retention, electrolyte imbalance and hypertension preclude liquorice from wider clinical use. The component in liquorice responsible for its mineral corticosteroidlike activity has been identified as glycyrrhizinic acid. A deglycyrrhizinized liquorice preparation (DGL) has been reported to retain the ability to accelerate the rate of healing of gastric ulcers in man[1] and to protect pylorus-ligated rats from ulcer formation[2]. The mechanism by which DGL prevents ulcer formation in Shay rats is unknown. ANDERSSON et al.[2] reported a decrease of the acid output in DGL-treated rats after a dose slightly higher than the one which reduced the number of ulcers formed. Since 24 h pylorus ligation seemed to be poorly suited for studies on the inhibitory effect of a single dose of DGL on acid output, we decided to repeat the experiments with rats carrying chronic gastric fistulas. In another group of rats, the effects on histidine decarboxylase (the histamine forming enzyme) in the gastric mucosa and on the concentration of immunoreactive gastrin in serum were studied.

Altogether 35 male Wistar rats weighing 150–250 g were used. Acid secretion was studied in 8 rats carrying chronic gastric fistulas[3]. The fistula rats were fasted for 24 h and then restrained in Bollman-type cages. The fistulas were opened and the stomachs rinsed with 0.9% saline until the return was clear. 10 ml 0.9% saline was given s.c. to replace fluid losses. After the fistula had been draining freely for 1 h, basal acid secretion was collected for two 1-h periods, after which DGL (kindly supplied by Dr S. ANDERSSON, Dept. of Pharmacology, Karolinska Inst., Stockholm) 200 mg/kg, suspended in 0.9% saline 40 mg/ml, was given i.p., and 4 further 1-h portions obtained. Acid output was determined by titration with 0.02*N* NaOH, using phenolphtalein as indicator. The same animals received the same volume of 0.9% saline (i.p.) in a control experiment.



Effect of deglycyrrhizinized liquorice (DGL), 200 mg/kg i.p., on gastric acid output in 8 chronic gastric fistula rats. DGL or 0.9% saline given as indicated by the arrow. Mean ± SEM. * $0.05 > P > 0.01$; ** $0.01 > P > 0.001$ and *** $P < 0.001$ according to Student's *t*-test.

Before determination of histidine decarboxylase activity and gastrin in serum all rats were fasted for 48 h. 12 normal and 8 antrectomized rats[4], were given 200 mg/kg DGL i.p. twice with 3 h interval. 7 normal control rats received saline only. 3 h after the last injection the animals were lightly anaesthetized with ether, the abdomen opened and blood drawn directly from the caval vein. The blood was allowed to clot at room temperature and the serum was freeze-dried. The concentration of immunoreactive gastrin was determined radioimmunochemically using rabbit antibodies against human serum gastrin[5] and a monoiodinated gastrin preparation [6]. Gastrin concentrations were expressed as pg equivalent of synthetic human gastrin I (SHG) per ml serum. Previous studies showed that gastrin in rat serum was measured with an accuracy similar to that in human serum[7]. Immediately after exsanguination the stomach was removed, cut open along the greater curvature and rinsed in ice-cold saline. The mucosa of the oxyntic gland area was scraped off and homogenized in 0.1*M* phosphate buffer, pH 6.9, to a final concentration of 100 mg wet weight /ml. After centrifugation at 10,000 × *g* for 15 min at 0 °C, the histidine decarboxylase activity in the supernatant was determined by incubation with ^{14}C-carboxyl-labelled histidine[8]. The enzyme activity is expressed as pmoles CO_2 formed per mg mucosa and hour.

The i.p. injection of DGL in a dose of 200 mg/kg caused a marked and highly significant reduction of the acid

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