Effect of reserpine on liver tyrosine-α-ketoglutarate transaminase in the rat

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THE demonstration that tryptophan pyrrolase activity of rat liver increases several-fold after administration of corticoid hormones or after stressful situations,[1] has led many authors to use this test as a tool for studying the drug-induced adrenal cortex stimulation.[2, 3] However, the fact that tryptophan pyrrolase rise may be induced not only by adrenal cortex activation but also by substrate administration,[4] renders the study of this enzyme unsuitable for the purpose outlined above.

The tyrosine-α-ketoglutarate transaminase (TKT) test seems to be more specific for studying the adrenal-dependent induction, as its increase may be induced only by corticoid administration[5, 6] while substrate administration acts only as a non-specific adrenal stimulation agent.

The present report deals with the activity of reserpine on liver TKT in the rat *in vivo*.

TABLE 1. LIVER TYROSINE-α-KETOGLUTARATE TRANSAMINASE 6 HR AFTER VARIOUS DOSES OF RESERPINE INTRAPERITONEALLY

(Enzyme activity: μmole of *p*-hydroxyphenylpyruvate (100 mg ww) 1 hr, with or without pyridoxal-5-phosphate, 30 μg.)

Treatment*	Tyrosine-α-ketoglutarate transaminase†	
	−Py	+Py
—	7·05	12·2
Reserpine 0·5 mg/kg	5·9	12·2
Reserpine 1 mg/kg	12·3	25·0
Reserpine 5 mg/kg	16·0	30·9

* 6 hr before killing.

† μmole *p*-OH-phenylpyruvate (100 mg ww) 1 hr.

EXPERIMENTAL

Male white rats weighing 200–250 g have been used.

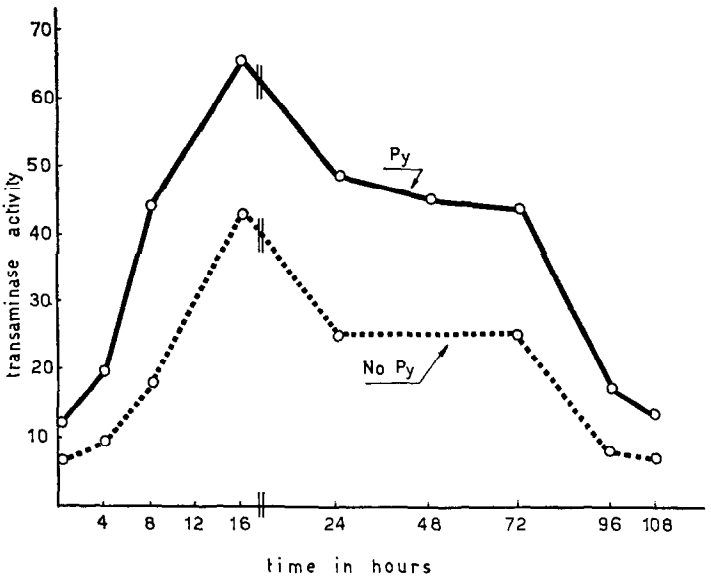

FIG. 1. Effect of a single dose of reserpine (5 mg/kg) on liver tyrosine-α-ketoglutarate transaminase as a function of time, in presence or not of pyridoxal-5-phosphate (Py). Enzyme activity expressed as micromoles of *p*-hydroxyphenylpyruvate (100 mg ww) 1 hr.

Reserpine (Serpasil CIBA) was injected intraperitoneally whilst control animals received an equivalent volume of saline.

TKT activity was determined in whole liver homogenate by the method described by Kenney.[7] In order to investigate better the enzyme-coenzyme saturation, the enzymic activity was measured with or without added pyridoxal-5-phosphate (Py).

RESULTS AND CONCLUSION

In Table 1 are presented the results of a dose-effect study. As it can be seen, reserpine increases the level of TKT several times: maximal elevation is obtained, in the time considered in this study, with 5 mg/kg of the alkaloid while a clear-cut response is observed with 1 mg/kg. Further results, not reported here, indicate that, with the smallest dose of reserpine, induction reaches its maximum after a longer delay.

The rise of TKT activity induced by reserpine is a long lasting effect as shown by the results presented in Fig. 1. With the rather high dose of reserpine used in this experiment, very high levels of TKT are still observed after 72 hr, and the enzyme activity is back to normal values after four days only.

This time curve is quite different from that which may be observed after a single injection of hydrocortisone[8] and differs as well from the time response of tryptophan pyrrolase to reserpine.

The fact that TKT activity is still elevated when both the pharmacological and the neurohormonal effects of reserpine have disappeared, is not easily understandable and may depend on the biochemical characteristics of the enzyme.

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The separation of synaptic vesicles from disrupted nerve-ending particles*

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WHEN guinea-pig brain is homogenized in 0·32 M sucrose, the nerve endings are torn away from their pre- and postsynaptic attachments to form nerve ending particles (NEPs), which can be isolated as a relatively pure fraction by differential and density gradient centrifugation.[1-3] This fraction is rich in bound acetylcholine (ACh),[4,5] choline acetylase (ChA)[4], hydroxytryptamine (HT)[5,6] and other amines. It also accounts for the 20 per cent of brain lactic dehydrogenase (LDH) which remains particle bound[7,8] on homogenization.

Using LDH as a marker for the soluble cytoplasm entrapped with NEPs, Johnson and Whittaker[7,8] compared the release of LDH and ACh brought about by disruptive procedures. Suspension of NEPs in hypo-osmotic solutions liberated up to 80 per cent of LDH but only 50 per cent of ACh,

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