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EFFECT OF 6-HYDROXYDOPAMINE ON ORNITHINE DECARBOXYLASE ACTIVITY IN CENTRAL MONOAMINERGIC SYSTEMS OF RAT

Marie-Françoise Belin and Jean-François Pujol
Département de Médecine Expérimentale, Université Claude-Bernard,
69373 LYON Cédex 2 - France

Recent studies have suggested that ornithine decarboxylase (ODC) could be an important regulatory enzyme in cellular metabolism. High ODC activities have been reported to be associated with cell proliferation [1,2,3,4] or induction of enzymes [5] suggesting a role for this enzyme in the control of protein synthesis. In adult rats ODC activity has been found to be very low in various brain structures [6]. In a recent study we have reported that reserpine treatment could induce an important stimulation of ODC activity in certain brain nuclei [7]. Destruction of catecholamine (CA) systems by 6-hydroxydopamine (6-OHDA) is followed by important variations of monoamine (MA) metabolism in some brain regions containing specific MA neurons [8,9]. This preliminary study reports a possible alteration of ODC activity in these systems after 6-OHDA treatment.

Male rats (OFA) (180-200 g) had access to standard diet and water ad libitum until 12 hours before 6-OHDA treatment. 20 µl Ringer solution with 0,1 % ascorbic acid was used as the vehicle for drug administration. The intracisternal injection of 6-OHDA (350 µg as free base) was performed under slight ether anesthesia to keep the same experimental conditions previously used in our metabolic studies [9]. To prevent 6-OHDA effects on catecholamine (CA) neurons some rats were pretreated with an intra-peritoneal injection of desmethylimipramine (Pertofran, Geigy) 25 mg/kg, 1 h before Ringer or 6-OHDA injections. Four groups of rats were used. Sham rats received Ringer solution alone (Group 1); treated rats (Group 2) received 6-OHDA ; some sham rats were pretreated with DMI (Group 3) and some of the 6-OHDA treated rats also received DMI (Group 4). Normal rats without any treatment were used as control. Tissue samples were taken at 4°C from different brain areas (locus coeruleus, raphe dorsalis nucleus, hippocampus and cortex) as previously described [7,10,11]. Samples from 8 rats were pooled and homogenized by sonification in 10 volumes of sodium potassium phosphate buffer (62.5 mM pH 7.2) with dithiothreitol (1.25 mM) pyridoxal phosphate (0.5 mM) and ethylenediamine tetra-acetic acid (62.5 µM). Aliquots of the homogenates were used for protein determination [12]. Homogenates were centrifuged at 10,000 g for 10 min. The ODC assay was carried out using the supernatant fractions by measuring $^{14}CO_2$ formation [4,13]. Samples contained 1 µCi of DL-(1-^{14}C) ornithine (ORN) (final concentration of L-ORN 47.5 µM). Incubations were carried out for 60 min at 37°C. The enzymatic reaction was stopped by addition of 100 µl of 4N H_2SO_4. Supernatant boiled in water bath (60 min) was used for the blank.

It was possible to detect ODC activity (1.5-2 times blank value) in every area studied by pooling microstructures from 8 rats (Table 1). Sham injected rats exhibited a short lasting increase of ODC activity in locus coeruleus and raphe dorsalis nucleus compared to controls. 5 and 8 h after injection, ODC activity had returned to control values. This effect could be a result of stress produced by our experimental condition. Both ether anesthesia and stress have been found to produce rapid metabolic activation of monoaminergic systems [14,15] and the increase in ODC activity could reflect this stimulation.

		3H	5H	8H
LOCUS COERULEUS	Controls	100 ± 9 (2)	100 ± 9 (2)	100 ± 9 (2)
	Sham	600 ± 100 (3) ★	110 ± 20 (2)	120 ± 10 (2)
	6OHDA	400 ± 20 (3) ★	340 ± 50 ★ (2)	300 ± 50 (2)
RAPHE DORSALIS	Controls	100 ± 10 (2)	100 ± 10 (2)	100 ± 10 (2)
	Sham	700 ± 50 (3) ★	130 ± 20 (2)	110 ± 9 (2)
	6OHDA	380 ± 40 (3) ★	240 ± 40 ★ (2)	170 ± 20 (2)
[illegible]	Controls	100 ± 8 (2)	100 ± 8 (2)	100 ± 8 (2)