Norepinephrine and Dopamine Concentrations in the Cerebral Cortex of Man, Monkeys and Other Mammals

Recently, THIERRY et al.[1] have shown that cortical dopamine (DA) in the rat cortex does not decrease after electrolytic or chemical (induced by 6-OH-dopamine) lesions of the ascending noradrenergic pathways; these lesions, on the other hand, cause a marked decrease in cortical norepinephrine (NE) content. These authors suggest that most cortical DA is not localized in noradrenergic nerve terminals, but in dopaminergic neurones, where it acts as a neurotransmitter.

We have previously reached similar conclusions[2] by observing that, in different brain areas outside the nigro-striatal pathway, DA can be depleted by reserpine, and has a synthesis rate higher than that of NE in the same areas.

In order to clarify whether the results obtained in rats might have a general significance, we have compared the concentration of NE to that of DA in the cortex of different animal species, including man. The results show that the concentration of DA is equal to or higher than that of NE, and support the hypothesis that the primary role of DA in the cortex is not as a precursor for NE, but as a neurotransmitter.

Materials and methods. Human cortical specimens were obtained bioptically from 7 male patients aged from 9 to 61 years; 4 operated on for brain injury, and 3 for brain tumors (2 gliomas, 1 meningioma). The brain of a 25-year-old man, killed in a car accident, was also removed in the autopsy room 12 h after death.

Animals used were: Wistar rats, weighing 250–280 g, cats weighing 3.5–4.0 kg and 2 Rhesus monkeys weighing 3.4 and 4.5 kg; all male. Rats were killed by guillotine; cats and monkeys were decapitated under pentobarbital anesthesia. The brain tissues were immediately dissected at 4 °C, frozen in dry ice and stored at −60 °C until analyzed. DA and NE were measured according to the method of LAVERTY and TAYLOR[3].

Results. Table I shows that catecholamines are present in the cerebral cortex of all animal species examined. While in rats the concentration of DA is roughly equal to that of NE, in the other species DA concentration is higher than that of NE. In the human cortex, the concentrations of DA and, in particular, NE are much lower than in the other species examined, including the monkey.

In the last 2 biopsies reported in Table I, the concentration of NE was below the sensitivity of the assay method, and that of DA was the lowest amongst the samples analyzed. This finding might depend on the presence in these subjects of a brain tumor which might have caused neuronal degeneration.

In the human brain removed autoptically, the concentration of NE and DA did not differ significantly in different cortical areas, and furthermore, the absolute values were not lower than those present in cortical specimens obtained bioptically.

As Table II shows, the administration of reserpine produced a marked depletion in NE and DA content in the rat cortex. These results confirm our previous finding that cortical DA is contained in reserpine-sensitive storage sites[2].

Conclusion. The presence of DA in the cortex in concentrations equal to or higher than that of NE suggests that DA in this area is not only the precursor of NE, but acts as a neurotransmitter. This hypothesis is supported by the findings of THIERRY et al.[1], TAGLIAMONTE and GESSA[2] and by the present results showing that cortical DA is contained in reserpine-sensitive storage sites. In fact COSTA et al. have shown that the fraction of DA which acts as precursor of NE is resistant to the reserpine action[4].

The physiological significance of cortical DA is not clear at present, however the presence of DA in the cortex in different species should be taken into consideration when considering the role of this amine in the psychostimulant effect of amphetamines, in the antipsychotic effect of neuroleptics, in the pathogenesis of depression or mania and, in general, in the modulation of mood, attention, aggressivity, motivation and many other

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Table I. DA and NE content in the cerebral cortex of different animal species

Species (No. of subjects)	DA (μg/g)	NE (μg/g)	Observations
Rat (6)	0.48 ± 0.03	0.40 ± 0.02	
Cat (6)	0.45 ± 0.04	0.21 ± 0.03	
Rhesus monkey (2)	0.41 ± 0.05	0.29 ± 0.02	
Man (8)	0.19	0.04	Biopsy–parietal, brain injury
	0.16	0.04	Biopsy–temporal, brain injury
	0.12	0.05	Biopsy–frontal, brain injury
	0.08	0.03	Biopsy–frontal, brain injury
	0.07	0.01	Biopsy–glyoma fronto-parietal
	< 0.01	< 0.01	Biopsy–glyoma temporal
	< 0.01	< 0.01	Biopsy–meningioma parietal
	0.18	0.05	Autopsy–pool from different cortical areas

For each analysis in the rat, the whole cortices from 3 animals were pooled. Since the experiments showed no significant differences in the catecholamine values of different cortical areas, these values were pooled averaged.

Table II. Effect of Reserpine on DA and NE content in the rat cortex

Treatment (mg/kg i.p.)	Rat cortex DA (μg/g)	NE (μg/g)
None	0.44 ± 0.03	0.38 ± 0.06
Reserpine 5	0.25 ± 0.01 [a]	0.08 ± 0.08 [a]

Each value is the average ± S.E. of at least 15 determinations. Reserpine was given 2 h prior to sacrifice. [a] $P < 0.01$ in respect to control values.

aspects of behavior. On the other hand, the finding that the human cortex has the lowest catecholamine concentration amongst the species analyzed, should be kept in mind when considering the role of these amines in memory and intellectual functions[5,6].

Riassunto. Nella corteccia di uomo la dopamina (DA) è presente in concentrazioni quattro volte maggiori della noradrenalina (NA). Nella scimmia, nel gatto e nel ratto il rapporto DA/NA è rispettivamente di 1.5:1, 2:1 e 1:1. Nel ratto la DA corticale è depletata dalla reserpina.

G. L. GESSA, G. BIGGIO, L. VARGIU, F. NAPOLEONE[7] and A. TAGLIAMONTE

Istituto di Farmacologia and Divisione di Neurochirurgia, Università di Cagliari, Via Porcell 4, I-09100 Cagliari (Italia), 27 May 1974.

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[7] Università di Cagliari, Divisione di Neurochirurgia, Via Porcell 4, Cagliari (Italy).

Radiometric Estimation of the Amount of Solid Gastrointestinal Contents

In studies on body composition in vivo, unknown and varying amounts of gastrointestinal (GI) contents present a main source of sytematic errors, especially when large ruminants are used[1]. Therefore, it has been investigated whether the volume of GI tract contents, i.e. dry matter and fresh minus dry matter (water) of the solid or liquid phase, can be estimated by dilution techniques employing radioactive markers.

For the experiments, 78-week-old bulls were used. As marker of the solid phase ^{152}Eu was employed since this radionuclide indicated no measurable radioactivity in the supernatant of the ruminal contents after centrifugation (30,000 × *g*, 10 min) and about 100% recovery in the feces[2]. The liquid phase was marked by ^{14}C-PEG. Inactive polyethylene glycol 4000 (PEG) as carrier similar in amounts to those in turbidity measurements[3] was added to the radioactive tracer because PEG in low concentrations tended to be adsorbed to intestinal contents[4]. The

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Radiometric (in vivo) and gravimetric (post mortem) estimations of gastrointestinal contents (dry matter, DM) in twelve 78-week-old bulls

Weight of bulls (kg)	DM intake per unit time [b] (kg/h)	^{152}Eu measurements			Dry matter contents (kg)					
		Delay time (h)	Turnover rate k_f (h^{-1})	Concentration C_o at $t = 0$ $\left(\frac{\text{ppm}}{\text{g DM}}\right)$	Rumen		GI tract		Intestine	
					post mortem	in vivo	post mortem	in vivo	post mortem	in vivo
456 [a]	0.264	10	0.0466	3635 [a]	5.48	5.92	7.95	8.94	1.29	0.28 [a]
405	0.126	10	0.0390	2316	3.02	3.23	3.90	4.48	0.44	0.43
526	0.333	6	0.0484	1099	6.42	6.88	8.59	8.88	0.93	0.91
420	0.275	11	0.0428	1223	6.86	6.43	8.85	9.45	0.92	0.82
463	0.300	7	0.0484	1193	5.73	6.20	7.40	8.29	0.82	0.84
483	0.303	5	0.0582	1477	5.13	5.21	6.36	6.72	0.84	0.68
555	0.361	6	0.0614	1361	5.88	5.88	8.19	8.06	0.99	0.74
550	0.351	6	0.0598	1309	8.00	5.87	9.55	7.98	0.83	0.76
450	0.305	6	0.0501	1393	5.80	6.09	8.13	7.92	0.86	0.72
505	0.318	6	0.0627	1708	5.56	5.07	7.03	6.97	0.89	0.59
524	0.347	10	0.0777	1956	5.90	4.99	7.99	7.94	1.12	0.51
538	0.326	9	0.0550	1187	6.46	5.93	8.39	8.86	1.05	0.84

[a] Reduced feed intake and diarrhea from 28 to 53 h post dosing. [b] Average totals for 6 days.