5-Hydroxyindoleacetic acid and homovanillic acid in cerebrospinal fluid and brain of different rabbit breeds after treatment with probenecid

In the rat brain stem the concentration of 5-hydroxytryptamine (5-HT) and its acid metabolite 5-hydroxyindoleacetic acid (5-HIAA) are of nearly equal magnitude. A rise of the 5-HIAA concentration after treatment with probenecid was explained as a sign of an active transfer mechanism for 5-HIAA (Neff, Tozer & Brodie, 1964; Werdinius, 1967). On the other hand, that probenecid increased the homovanillic acid (HVA) concentration threefold (Werdinius, 1967) suggested that, in the rat caudate nucleus, the tenfold difference in the concentration of dopamine compared to HVA was a sign of the existence of an active transfer mechanism for HVA. We had previously found that probenecid did not increase the concentration of 5-HIAA and HVA in the central nervous system (cns) of the rabbit, while Bowers (1970) had shown 5-HIAA was increased in both brain and cerebrospinal fluid (csf) after administration of probenecid.

We therefore gave probenecid (200 mg/kg i.v.) to 60 rabbits of three different breeds, the domestic white rabbit, the Dutch rabbit, and a rabbit, which was mostly a cross between Havana, Belgian giant and Little Silver. HVA was measured in the cisternal csf and brain (Korf, Roos & Werdinius, 1971), 5-HIAA in the brain (Jonsson & Lewander, 1970) and in the csf (Sharman, 1960). The brain of one rabbit could be used for both acids. For HVA the caudate nucleus and putamen were removed in one piece as a corpus striatum. The brain stem was used to measure 5-HIAA.

Our normal values (Table 1) differ from those of Bowers (1970), who used New Zealand white rabbits. We found equal doses of probenecid to elicit different results in different breeds (Fig. 1, A–B).

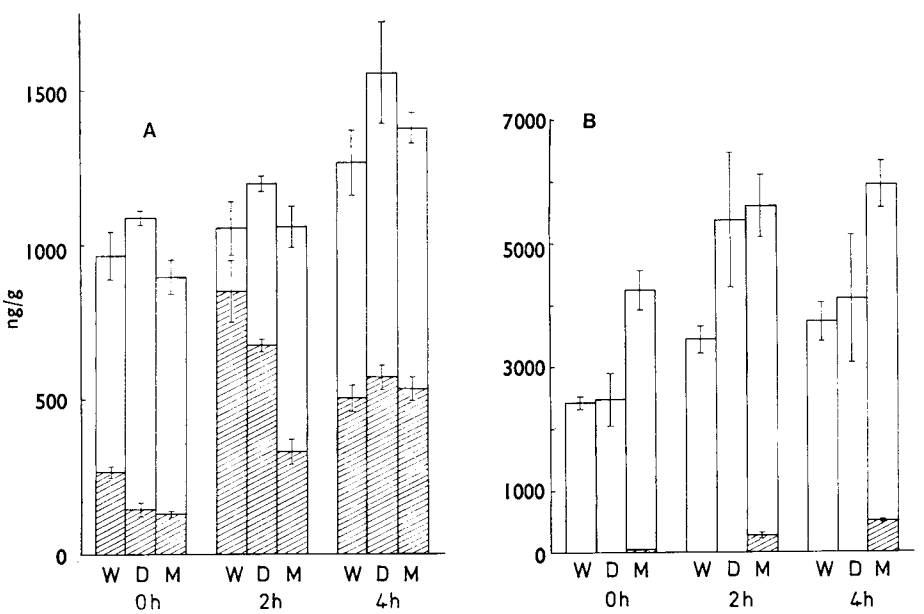

FIG. 1. Values of 5-HIAA (A) and HVA (B) in brain (open bars) and csf (hatched bars) 0 to 4h after 200 mg/kg probenecid to white (W), domestic (D) and mixed (M) rabbits. Values are means ± s.e. in ng of the acid per g of brain or ml of csf.

Table 1. *Normal values of 5-HIAA and HVA in cisternal csf and brain in rabbits of different breeds.*

	5-HIAA*			HVA*		
Breed	Csf	Brain	Csf: brain	Csf	Brain	Csf: brain
Domestic white	266 ± 19	965 ± 77	0·29	n.d.	2429 ± 103	
Dutch	144 ± 21	1088 ± 23	0·13	n.d.	2485 ± 426	
Mixed breed	128 ± 10	897 ± 56	0·14	45 ± 9	4243 ± 309	0·01

* Values are means ± s.e. in ng of the acid per ml of csf or g of brain.

The time lag seems to be an important factor. The reason why our earlier experiments failed to show any rise in 5-HIAA in the brain 2 h after probenecid might be that in the white rabbit the increase seems to be less pronounced than in some other breeds, and would not be evident until approximately 4 h after injection of the drug ($P < 0.05$). There seems also to be a difference between breeds of rabbits. The increase of 5-HIAA in the brain of Dutch rabbits was not statistically significant, while that of mixed breed ("mongrel" in Fig. 1, A–B) showed a highly significant increase ($P < 0.01$). HVA concentrations in brain are significantly different from controls in white rabbits after 2 h ($P < 0.001$) and mixed breed rabbits ($P < 0.005$). In all breeds 5-HIAA and HVA in csf increased significantly. The response could also be related to dosage of probenecid and different rates of metabolism in the different breeds, a possibility now being investigated.

When these experiments were in progress, our attention was drawn to an article by Cserr & van Dyke (1971) presenting strong evidence for an active transport mechanism for 5-HIAA in the rabbit.

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