Effects of dopamine, noradrenaline and 5-hydroxytryptamine on the cerebral blood flow in the dog

I have examined the effects of several biogenic amines on the cerebral blood flow in the dog.

The experiments were made on lightly anaesthetized artificially ventilated dogs. The cerebral blood flow measurements were made using the radioactive gas elimination method of Lassen, Høedt-Rasmussen & others (1963) according to Häggendal, Nilsson & Norbäck (1965). The amines were administered by continuous intravenous insution; the dose was altered by changing the infusion rate.

Noradrenaline was infused in doses varying from 0·03 to 7·5 μg/kg min. Noradrenaline induced a reduction of the cerebral blood flow, that seemed to be maximum at an infusion rate at 2 μg/kg min. The maximum flow reduction from the control values was about 21%, which is significant at $P = 0{\cdot}01$. The flow reduction was blocked by the peripherally acting α-adrenoceptor blocking agent, phentolamine, administered intravenously. The cerebral metabolic rate for oxygen was fairly constant.

5-Hydroxytryptamine (5-HT), was similarly infused in doses from 0·1 to 22·8 μg/kg min. 5-HT also reduced the cerebral blood flow significantly ($P < 0{\cdot}01$) by about 28%. The cerebral metabolic rate for oxygen was constant. The reduction of cerebral blood flow caused by 5-HT was not inhibited by peripherally acting α- or β-adrenoceptor blocking agents.

Dopamine infused in the same way in doses varying from 0·05 to 57·4 μg/kg min produced a biphasic response. During infusion with small doses, the animals showed a reduction in cerebral blood flow of about 20% (as during noradrenaline infusion); this reduction could be abolished by phentolamine. The cerebral metabolic rate for oxygen was not changed.

At higher infusion rates, however, dopamine induced a significant ($P < 0{\cdot}01$) *increase* of the cerebral blood flow of up to 30% of the control values. The cerebral metabolic rate for oxygen was constant. This increase in flow could be blocked by intravenous administration of pimozide or haloperidol but was not reduced by propranolol.

This finding is interesting when compared with the results of McDonald & others (1963) and Eble (1964), who found dopamine causes an increase of the blood flow through the kidney and the mesenterial vessels that could be blocked by haloperidol.

My findings may be of importance for the understanding of some circulatory disturbances of the brain and also for a correct interpretation of altered concentration of different amines, and their metabolites, in brain tissue and cerebrospinal fluid after administration of certain biogenic amines or their precursors.

Departments of Neurosurgery,
Clinical Physiology, and Pharmacology,
University of Göteborg, Sweden.

CLAES VON ESSEN

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REFERENCES

EBLE, J. N. (1964). *J. Pharmac. exp. Ther.*, **145**, 64–70.

HÄGGENDAL, E., NILSSON, N. J. & NORBÄCK, B. (1964). *J. clin. Invest.*, **43**, 1116–1124.

HÄGGENDAL, E., NILSSON, N. J. & NORBÄCK, B. (1965). *Acta physiol. scand.* **66**, *Suppl.* **258**, 5–25.

LASSEN, N. A., HØEDT-RASMUSSEN, I., SØRENSON, S. C., SKINHØJ, E., CRONQUIST, S., BODFORSS, B. & INGVAR, D. H. (1963). *Neurology* (*Minneap.*), **13**, 719–727.

MCDONALD, R. H. Jr., GOLDBERG, L. I., MCNAY, J. L. & TUTTLE, E. P. Jr. (1963). *Clin. Res.* **11**, 248.