Acta vet scand. 1984, *25*, 600—602.

Brief Communication

INCORPORATION OF ^{3}H-DETOMIDINE IN THE BRAIN TISSUE OF THE RAT. AN AUTORADIOGRAPHIC STUDY

Detomidine (4(5)-(2.3-dimethylbenzyl)imidazole) hydrochloride is a recently developed sedative-tranquillizing agent, which is therapeutically valuable in veterinary medicine (*Alitalo & Vainio* 1982 a and b, *Vainio* 1982). It is shown to be useful especially in the treatment of horses, cattle, and sheep. Its clinical effect is a strong decrease of fright and agitation. Furthermore, detomidine has a strong analgetic effect. The laboratory studies have shown that detomidine is a potent alfa-adrenoceptor, especially alfa$_2$-adrenoceptor, agonist (*McDonald* 1983). It has been shown biochemically, that detomidine is absorbed rapidly from the injection site even after subcutaneous administration. Also the distribution in the brain tissue is rapid. Attempts to localize the incorporation of detomidine in different parts of the brain have not been made so far. The aim of this autoradiographic work was to study the distribution of injected ^{3}H-labelled detomidine in the brain tissue of rats.

Male Fisher rats weighing 185—195 g were used. All rats were kept in the same room, they received a standard pellet diet and tap water ad libitum. The material consisted of 20 rats. The rats were injected intraperitoneally or intraveneously. The solution injected contained ^{3}H-detomidine hydrochloride 220 μg/ml and detomidine hydrochloride 200 μg/ml*. Activity per ml was 1.4 mCi. According to the HPLC analysis made on the ^{3}H-detomidine, the purity, expressed as a percentage, exceeded 90. The injection volume varied between 0.1 and 1.0 ml.

The rats were killed by rapid decapitation without anaesthesia. Decapitation was performed 1 to 20 min after the injection. The brains were fixed in Bouin's fluid and embedded in paraffin. Serial sections were made at 8 μm. Autoradiograms were made by the dipping technique, using Kodak NTB 2

---

* Detomidine and ^{3}H-detomidine were provided by the manufacturer of detomidine Farmos Group Ltd, Turku, Finland.

emulsion. The slides were stored in light-proof boxes with calcium chloride as dehydrating agent for 1—90 days at +4°C, developed in Kodak D 11 developer, and fixed with Kodak rapid fixer. The sections were stained with haematoxylin-eosin.

In the autoradiograms, a great number of silver grains was observed in the brains of the animals as early as 1 min after the injection of labelled detomidine. In the brains of rats injected with large dosages, the incorporation was very massive. The grains were seen in every structure of the central nervous system. The most intensive incorporation of tritium appeared in the gray matter. Even if a systematic grain counting was not made, the incorporation of tritium was especially intensive in the neurons of the cerebral and cerebellar cortex, in the ganglionic layer of the hippocampus, in the basal ganglia, in the parvocellular as well as the magnocellular part of the hypothalamus, and in the formatio reticularis. It must be emphasized, however, that the differences in the number of grains were not great in the various parts of the brain. The mural ependyma seemed to be almost without grains.

Based on these observations, it can be stated that the absorption of detomidine into the brain is very rapid. This drug seems to have a strong ability to penetrate the blood/brain barrier. The incorporation was very even, being most intensive in the gray matter. It was not possible to point out any special brain structures which could be interpreted as target areas for the activity of detomidine.

The results must be considered bearing in mind the limitations which generally apply to autoradiographic studies. Primarily, these considerations concern the question whether the localization of the label is the same as the localization of the labelled drug in the tissue. Rapid metabolic processes can interfere with studies of this kind, by detaching the label from the labelled drug.

J. Kuussaari, L. A. Lindberg and *S. Talanti*
The Department of Anatomy and Embryology,
College of Veterinary Medicine, Helsinki, Finland.

REFERENCES

Alitalo, I. & O. Vainio: The effect of a new tranquilizer detomidine, in horses. Proc. 1st Int. Congr. Vet. Anaesth., Cambridge 1982 a, p. 222—225.

Alitalo, I. & O. Vainio: Detomidine as a sedative and premedicine in large animals. A clinical study in horses and cattle. Proc. 14th Europ. Soc. Vet. Surg. Congr., Istanbul 1982 b, p. 69—75.

MacDonald, E.: Alpha-2-adrenoceptor stimulation by detomidine in rats. Progr. Neuro-Psychopharmacol. Biol. Psych., Suppl. 1983, 212. (5th CA Symposium, Göteborg).

Vainio, O.: Detomidine hydrochloride. A novel imidazole-type sedative analgesic. Proc. 2nd Europ. Ass. Vet. Pharmacol. Toxicol., Toulouse 1982, p. 798—799.

(Received December 27, 1984).

Reprints may be requested from: S. Talanti, the Department of Anatomy and Embryology, P. O. Box 6, SF-00551 Helsinki, Finland.