PENTOBARBITONE ANAESTHESIA IN AN ANIMAL MODEL OF HUNTINGTON'S DISEASE

Sir,—Kainic acid (KA) injections to the rat striatum produce severe loss of striatal neurones, leaving intact both afferent nerve terminals and traversing fibres. The biochemical, morphological and behavioural alterations of KA-injected rats appear to be similar to those found in patients with Huntington's disease (HD) (Coyle et al., 1978; Sanberg, Pisa and Fibiger, 1979; Pisa, Sanberg and Fibiger, 1980). Furthermore, the responses to various pharmacological agents elicited in these rats is similar to the responses seen in patients with HD (Mason, Sanberg and Fibiger, 1978). Therefore, this animal syndrome appears suitable for evaluating the effectiveness of various therapeutic agents for possible use in HD patients.

An enhanced sensitivity to anaesthetic drugs in patients with HD was reported by Davies (1966) and Guandalini and Bonfanti (1968), but Farina and Rauscher (1977) were unable to confirm this. Using the KA animal analogue of HD, we were interested in determining the response of these animals to pentobarbitone anaesthesia.

Male Wistar rats, weighing about 300 g, were injected stereotactically with KA 3 nmol in phosphate-buffered saline 0.5 μlitré (pH7.2) to both striata as described elsewhere (Sanberg, Pisa and Fibiger, 1979; Pisa, Sanberg and Fibiger, 1980). Control rats received the injections of phosphate buffered saline only. About 3 months later the rats were injected with sodium pentobarbitone either 50 mg kg⁻¹ or 100 mg kg⁻¹ i.p. in a volume of 1 ml kg⁻¹. Measurements included latency to first motor effect (staggering, falling or no-righting response), latency to immobility (no movement for at least 20 s), latency to disappearance of tail reflex (elicited by gently squeezing a haemostat on the end of the tail every 15 s), and latency to disappearance of corneal reflex (elicited by gently touching the cornea every 15 s with a few strands of cotton). Immediately after behavioural testing, each animal was subjected to intracardiac perfusion with isotonic saline solution followed by 10% formol saline and the brain was removed for histological analysis (Sanberg, Pisa and Fibiger, 1979; Pisa, Sanberg and Fibiger, 1980).

The results are shown in table I. KA rats showed significantly shorter latency to first motor effects (t = 2.66, d.f. = 33, P < 0.02) and immobility (t = 2.96, d.f. = 33, P < 0.01), compared with controls, following administration of sodium pentobarbitone 50 mg kg⁻¹. However, rats did not differ in their latency to the tail or corneal reflex tests (P > 0.05), compared with control, at either dose of sodium pentobarbitone. At 100 mg kg⁻¹ of sodium pentobarbitone the KA rats showed a significantly shorter latency (t = 2.29, d.f. = 15, P < 0.04) to first motor effects than control, but did not differ significantly in the immobility test (probably because of a ceiling effect).

These results demonstrate that rats with KA-induced striatal lesions show an enhanced sensitivity to the motor inhibiting effects of pentobarbitone, but not to the inhibitory effects on corneal or pain reflexes. These findings suggest that HD patients may have enhanced sensitivity to the motor inhibiting effects of sodium pentobarbitone, but not to the anaesthetic effects of this drug. On anaesthetizing patients with these or similar disorders it could be misleading to interpret an abnormally fast induction of motor depression as an index of increased sensitivity to the anaesthetic effects of sodium pentobarbitone.

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REFERENCES

Table I. Effect of striatal lesions induced with kainic acid on latency to the motor inhibiting and anaesthetic effects of sodium pentobarbitone. Mean ± SEM for n rats in each group. † Included are staggering, falling, and lack of righting responses. Significantly different from controls: *P < 0.05; **P < 0.01.