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Pentobarbitone distribution in various regions of the rat brain in relation to the kinetics of its effect

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The radioactivity of rat brain was measured at various intervals (5, 10, 15, 20, 30, 40, and 70 min) after intraperitoneal administration of 14 C-labelled pentobarbitone (20 μ c/kg) together with unlabelled pentobarbitone (62 mg/kg). The brain was carefully dissected, and pieces of nervous tissue were sampled. The regions studied were as follows: frontal, parietal and occipital cortex, fornix and nucleus caudatus, anterior and posterior thalamus, rostral and caudal hypothalamus, ventral mesencephalus, anterior and posterior colliculi, pons, cerebellar hemispheres and vermis, medulla oblongata and cervical spinal cord.

Close agreement was observed between the overall time-course of the distributions and that of its concentration on the receptor biophase, as determined from the times of the disappearance and reappearance of the righting reflex (Palumbi, Rossini & Segre, 1966; Giorgi, Palumbi, Rossini & Segre, 1966). The highest activity was reached after 20 min in the inferior posterior nucleus of the hypothalamus. This area does not appear to have an especially high blood flow, as evaluated with ¹³¹I-labelled serum albumin (150 μ c/kg, i.v.). The inferior posterior basal ganglia showed a much higher concentration than the other regions when incubated for 20 minutes at 37° C in oxygenated Krebs-phosphate medium containing non-labelled pentobarbitone at 62 mg/l. and labelled pentobarbitone with an activity of 20 μ c/l.

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A metabolic explanation for differences between species of the anticonvulsant activity of diazepam

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A selective activity against metrazol-induced convulsions is a characteristic property of benzodiazepines, although species differences have been observed. The anticonvulsant activity of diazepam (5 mg/kg intravenously) in respect to metrazol (100 mg/kg, intraperitoneally) disappears in rats after 6 hr while it is present in mice for about 24 hr. Furthermore diazepam (5 mg/kg) antagonizes a higher dose of metrazol in mice (300 mg/kg) than in rats (150 mg/kg).