values, and are raised to 128% of normal in the hind-brain, after administration of 60 mg/kg of leptazol producing 100% clonic convulsions. It is concluded that AA is catabolized in the mid- and fore-brain, and is absorbed into the hind-brain, during clonic and tonic convulsions. Under normal circumstances brain AA is retained in a stable pool. This cannot be depleted by convulsions in combination with a scorbutogenic diet. Deficiency of AA exacerbates, and raised brain AA reduces, frequency and incidence of seizures. It is suggested that AA may play a major metabolic role in the brain.

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Uptake of propranolol by the isolated perfused rat liver

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In the isolated perfused rat liver, propranolol at low concentrations was almost completely extracted from the perfusion fluid at the 'first pass' through the liver. This is in agreement with the work of Shand and co-workers. The extraction ratio (E.R.) of the propranolol decreased from 0.96 to 0.68 as the propranolol concentration increased from 1-1000 μM. The percentage of unchanged propranolol remaining in the liver at the end of the perfusion period increased from 4 to 68% as the concentration increased from 1-1000 μM. This high clearance or 'first pass' effect of propranolol consists of both uptake and metabolism. A decrease in the metabolism and clearance of propranolol (1 μM) was observed at a lower perfusion temperature and during simultaneous perfusion with nortriptyline (100 μM) another drug known to exhibit the 'first pass' effect. However, in similar experiments with either the microsomal inhibitor SKF 525A (100 μM) or lignocaine (100 μM), which is also well cleared by the liver, selectively decreased the percentage of propranolol metabolized in the liver from 96% to 55% and 38% respectively, but was without effect on the clearance of the propranolol. P-hydroxyacetanilide (paracetamol) is also well cleared by the liver but had no effect on either the metabolism or the clearance of propranolol. It appears that the mechanisms of the high hepatic clearance and metabolism of several drugs such as propranolol, p-hydroxyacetanilide and lignocaine are different.

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