lactate accumulation rate in tris- or bicarbonate-buffered saline (10 and 30% respectively) with 25 mM-glucose 6-phosphate as substrate, caused a 37% decrease in the internal tissue glucose concentration in bicarbonate-buffered medium. Tissue glycogen concentration was unaffected. Insulin (0.01 i.u./slice) had no effect on tissue glucose concentration in bicarbonate-buffered saline. Since isolated synaptosomes, incubated for 1 h at 38°C in tris-buffered saline with 25 mM-glucose 6-phosphate, had a tissue glucose concentration (per mg of protein) some 10 times that found in slices under similar incubation conditions (glucose concentrations in the medium were similar), it is possible that a large part of the intracellular glucose pool may be located in nerve endings.

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Synaptosome Beds: a Method for the Study *in vitro* of the Metabolism and Function of Nerve Endings

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The functional unit of chemical transmission in the nervous system is the nerve ending. When cortex tissue is homogenized in iso-osmotic sucrose, the nerve endings seal off from the axon and may be prepared by sucrose-density-gradient centrifugation (Gray & Whittaker, 1962). Suspensions of nerve endings or synaptosomes exhibit the metabolic properties of cellular material, being able to carry out active glycolysis and oxidation of added glucose, linked to ATP and phosphocreatine production (Bradford, 1969).

When applied iontophoretically to the mammalian cerebral cortex, small concentrations of glutamate and aspartate cause excitation and γ -aminobutyrate causes inhibition of neuronal membranes (Krnjević & Phillis, 1963). Treatment of suspensions of synaptosomes with electrical pulses or elevated K^+ concentrations leads to a specific release of these three physiologically active amino acids (Bradford, 1970).

To decrease the large fluid/tissue ratio of the suspension to something more closely resembling that *in situ*, synaptosomes were sedimented on to nylon gauze, and a sandwich was formed by placing another piece of gauze on top. The resulting bed of synaptosomes could be easily manipulated and rapidly fixed at the end of incubation. This preparation

showed similar metabolic properties to synaptosome suspensions, glycolysing and oxidizing glucose with parallel formation of ATP and phosphocreatine. Application of electrical pulses stimulated O_2 uptake and glycolysis by 40% and oxidation of glucose to amino acids. Both electrical stimulation and elevated K^+ concentrations in the medium led to a significant increase in the release of glutamate, γ -aminobutyrate and aspartate into the medium, whereas the concentrations of other amino acids were not greatly affected.

On the inclusion of amino acid analogues of glutamate or γ -aminobutyrate in the incubation medium, increased concentrations of these amino acids were found in the medium, which indicated that uptake of these amino acids had occurred under normal conditions when the analogues were not present.

In the absence of Ca^{2+} , the release of glutamate, γ -aminobutyrate and aspartate in response to depolarizing influences was greatly decreased. When ethanedioxybis(ethylamine)tetra-acetate was included in the incubation medium containing no Ca^{2+} , the K^+ -stimulated release was totally inhibited. The presence of Na^+ at a concentration greater than 40 mM was found to be essential for maintaining the normal concentration of γ -aminobutyrate found in the synaptosome bed.

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Drug Interactions in Experimental Hepatic Porphyrin: a Model for the Exacerbation by Drugs of Human Variegate Porphyrin

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Human variegate porphyria is a genetically transmitted disorder characterized by excessive formation of porphyrins in the liver. There are latent phases of the disease during which porphyrins are excreted in excess and phases of exacerbation (or acute attacks) when excessive amounts of the porphyrin precursors 5-aminolaevulinic acid and uroporphobilinogen are also excreted together with even larger amounts of porphyrins (Dean & Barnes, 1959). The exacerbation of the metabolic disorder is usually brought about by barbiturates and other drugs (Eales, 1971), which do not alter significantly the porphyrin metabolism of normal individuals.

3,5-Diethoxycarbonyl-1,4-dihydrocollidine produces in experimental animals a hepatic porphyria