Some effects of phenobarbitone on the properties of synaptosomes

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The effects of anticonvulsant drugs on the brain *in vivo* have been attributed, at least in part, to direct physicochemical effects upon the neuronal cell membrane. The properties of membranes separating compartments of cerebral cortex slices incubated *in vitro* are apparently modified by phenobarbitone and other anticonvulsants so that the rates of transport of compounds across the membranes are altered (Gilbert, Ortiz & Millichap, 1966). The effects of phenobarbitone on the synaptosomal membrane may be of importance because the membrane has properties in common with cell membranes and because the synaptosome is believed to contain transmitter compounds.

Synaptosomes were prepared from guinea-pig cerebral cortex by the method of Gray & Whittaker (1962). The activities of succinic dehydrogenase and acetylcholinesterase and the respiratory rates of the preparations agreed with results published by other workers.

The effects of phenobarbitone on the shrinking and swelling of synaptosomes, at 25° C, in NaCl solutions of different osmolarities were determined by measuring changes in the extinctions of suspensions of the synaptosomes in the different solutions at 520 nm. Prior to this procedure the synaptosomes were pre-incubated for 30 min at 25° C in 0·32 M sucrose with or without phenobarbitone. The volumes of intact synaptosomes in the suspensions were taken as being proportional to the reciprocals of the extinctions of the suspensions (Keen & White, 1970).

On transfer from 0·20 M NaCl to 0·05 M NaCl the increase in volume of the synaptosomes was in agreement with the van't Hoff Law. Phenobarbitone (0·1 and 2·0 mM) caused significant increases ($P<0·05$ and 0·001, respectively; six experiments) in the volume of the synaptosomes in 0·20 M NaCl and significantly increased the change in volume occurring when the synaptosomes were transferred to 0·05 M NaCl ($P<0·05$ and 0·001, respectively; six experiments). The increase in the initial volume in 0·20 M NaCl was due to the prevention by phenobarbitone of shrinkage of synaptosomes during the pre-incubation in 0·32 M sucrose before transfer to the NaCl solution. Shrinkage of the synaptosomes may be due to the loss of low molecular weight compounds from the particles during the pre-incubation. Phenobarbitone may therefore prevent this loss. This conclusion is compatible with the observation that an increased level of ^{14}C-label was attained in synaptosomes incubated in media containing ^{14}C-glucose (U) and phenobarbitone (2 mM) over a period when neither sugar transport nor respiration appeared to be increased.

Phenobarbitone also prevented synaptosomes from returning so far towards their original volume as did control samples when the synaptosomes were transferred from 0·05 M to 0·20 M NaCl. This effect may be due to increased bursting of synaptosomes in 0·05 M NaCl when phenobarbitone is present.

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