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Effects of general anaesthetic agents on membrane conductance and surface potential

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Many general anaesthetics alter the ion permeability of biological and artificial membranes. The mechanisms whereby such alterations in permeability are effected are unclear at present. It is known, however, that anaesthetics affect the 'fluidity' of lipid bilayers and this action has been put forward as a means whereby they might alter membrane permeability, as discussed in formal thermodynamic terms by Hill (1974). Another way in which these drugs might change membrane conductance is by altering the potential at the surface of the membrane concerned. The electrostatic potential difference across the membrane/aqueous interface has been shown to be an important factor in the control of membrane conductance both in biological systems (Chandler, Hodgkin, & Meves, 1965) and artificial preparations (Haydon & Myers, 1973). This investigation is concerned with the extent to which anaesthetic-induced changes in membrane surface potential are responsible for changes in conductance observed.

The experimental preparations were artificial planar bilayer membranes (black lipid films) formed from a solution of glycerylmonooleate (7mM) in *n*-decane and rendered conducting by the presence of the potassium carrier nonactin. The drugs studied were *n*-alkyl alcohols. Addition of ethanol to the aqueous solution bathing the membranes (100mM-KCl) produced an increase in membrane conductance. Thus, for example, ethanol (0.7M) in the bathing solution reduced the specific membrane resistance by approximately one-third. If this conductance change were solely the consequence of an alteration in membrane surface potential induced by ethanol (i.e., if ethanol is only able to bring about conductance changes by altering membrane surface potential and has no effect on other membrane properties involved in the control of permeability), then the magnitude of the underlying potential change $\Delta(\Delta\emptyset)$ may be estimated using the following expression (from Hladky & Haydon, 1973):

$$-\frac{RT}{zF}\log_e\frac{G_2(O)}{G_1(O)}=\Delta(\Delta\emptyset)$$

where $G_1(0)$ and $G_2(0)$ are the specific membrane conductances (in the limit of zero applied potential) before and after addition of ethanol, z is the valence of the current-carrying ion, R is the universal gas constant, T is the absolute temperature and F is the faraday. Applying this equation to the present data, it can be seen that the addition of ethanol (0.7M) to the aqueous phase would be expected to reduce membrane surface potential by approximately 10mv (potential inside membrane shifted in negative direction). This would be sufficient to explain the increase in conductance observed. However, it is possible to *measure* the potential change evoked at a membrane/water interface by adsorption of ethanol and compare the experimental result with that predicted on the basis of conductance data. This was achieved here by determination of compensation potential changes for spread monolayers of glycerylmonooleate at an air/water interface on addition of ethanol to the aqueous phase. Monolayer measurements of this type are directly applicable to the bilayer systems used in the conductance estimations, as demonstrated by MacDonald & Bangham (1972). At concentrations in the range used in the bilayer studies, it was found that ethanol increased the surface potential of glyceryl-monooleate monolayers by more than 100mv (potential inside membrane shifted in positive direction). Accurate estimation of the potential increase was technically difficult because of the volatility of the drug under consideration. It is clear, however, that the observed surface potential change differs markedly from that expected on the basis of the bilayer conductance studies. Indeed, the compensation potential data

indicate that ethanol would be expected to reduce membrane conductance drastically if its effect on this parameter were solely the result of its action on membrane surface potential, whereas an increase in conductance is in fact observed. It is likely, therefore, that the gross effect of ethanol on membrane permeability is the complex result of this drug's action on a variety of underlying membrane properties, some of these factors acting in opposition to others in their control of membrane conductance. The techniques described here allow evaluation of the relative importance of one of these underlying factors (membrane surface potential) in anaesthetic action in relative isolation from the others. It is to be hoped that the use of such techniques will be extended to other drugs; study of a range of non-volatile anaesthetics would simplify interpretation of the compensation potential data.

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