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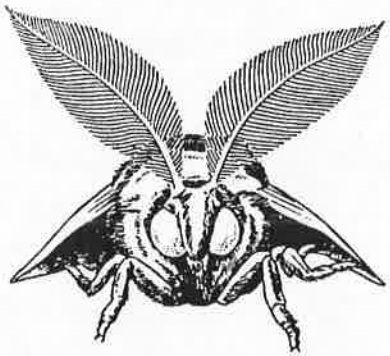

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Effects of volatile anaesthetics on cultured astrocytes from the rat cortex

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The state of general anaesthesia is linked to a depression of neuronal activity in the central nervous system. It was proposed (Nicoll et al., 1982, Science,217, 1055-6) that this is due to a hyperpolarization of cortical neurons. Although this hyperpolarization may be caused by the opening of neuronal potassium or chloride channels, a decrease in the extracellular potassium activity, which might occur during anaesthesia, provides an alternative explanation. Since glial cells regulate the ion composition of the extracellular space, we investingated the effects of the commonly used volatile anaesthetics (VAs) on the membrane potential and input resistance of cultured astrocytes which were isolated form the brains of young rats.

When enflurane was applied in a clinical range of concentration (n=35), the membrane potential of the cells, monitored in the patch clamp whole cell configuration, depolarized in a dose dependend manner. With 7 Vol% (4.2 MAC) the depolarization was as large as 43 mV. This effect was fully reversible. The depolarization was possibly due to the opening of large conductance anion channels, which were actived in isolated membrane patches during enflurane administration. However, at low concentrations, the cells either hyperpolarized or depolarized, indicating more complex actions on the cell membrane as to affect a single class of ion channels.

In contrast to enflurane, the VAs isoflurane (n=8)and halothane (n=17)were less effective in depolarizing glial cells even when applied at high concentrations. The variability concerning the alternations of the membrane potential was rather high. At low concentrations about 50 % of the cells either hyperpolarized or depolarized.

With all anaesthetics, the input resistance of astrocytes slightly decreased. However, this result is difficult to interpret, since astrocytes were coupled via gap junctions. VAs modulate this coupling as has been shown elsewhere (Mantz et al., 1993, Anesthesiol.,78, 892-901).

In summary, our results do not support the hypothesis, that glial cells contribute to the depression of neuronal activity by lowering the extracellular potassium activity. The effects do not follow the Meyer-Overton rule, which is a necessary criterion for effects to be relevant on the behavioural level. Assuming that astrocytes in vivo are affected in a similar manner as shown here, it must be concluded, that changes in the extracellular ion composition do occur under anaesthesia at least at high concentrations and with enflurane. Such changes will overlay with the direct actions of general anaesthetics on central neurons. When recording from such neurons in vivo or in slice preparations, the data should be interpreted with great caution, since effects which are not compatible with the Meyer-Overton rule may be introduced by actions of VAs on glial cells.