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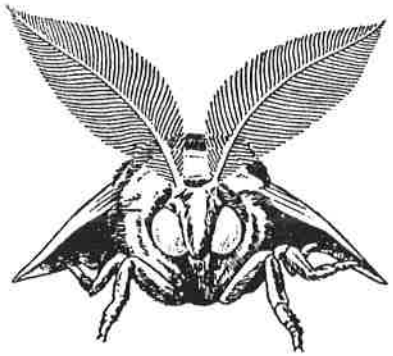

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Volatile anaesthetics depress neuronal activity in the mammalian CNS by enhancing GABAergic inhibition

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The state of general anaesthesia (GA), which is induced by a wide range of chemically different compounds, is not compatible with consciousness. However, during anaesthesia, acustic and visuell stimuli still reach the corresponding cortical fields, from where evoked potentials can be recorded. In the case of volatile anaesthetics (VAs), which are commonly used in surgery, the underlying cellular mechanisms are not well understood. Hippocampal and neocortical brain slices were prepared from rats and guinea pigs to analyse the effects of VAs on central neurons in vitro. Experiments were carried out on 26 cells either with sharp microelectrodes or with patch electrodes in the wohle cell configuration.

When recording from single pyramidal cells in the CA1 or CA3 region of the hippocampus, spontaneous activity was strongly reduced or completely abolished when enflurane, halothane or isoflurane were applied via bath perfusion. In silent neurons, current injections, which were sufficient to elict action potentials had to be largely increased until spikes occured, if VAs were present. This was mainly due to a decrease in the input resistance of the cells.

VAs frequently hyperpolarized (4mV +/-2mV SD, n=34) and in some cases depolarized (3mV +/-2mV, n=4) the hippocampal pyramidal cells. When the membrane potential was altered by continous current injections, these effects reversed around -70 mV, which is close to the Nernst potential of chloride ions.

The potency of VAs in reducing neuronal excitability was strongly reduced, if the slices were treated with the $GABA_A$ antagonist Bicuculline.

Comparing the action potentials in the presence and absence of VAs, the spike amplitude and threshold stayed unaffected. The risetime was slightly prolonged and the spike afterhyperpolarization strongly reduced.

With all anaesthetics similar effects were observed, when applied at 2 times the minimal alveolar concentration (MAC). 1 MAC is defined as the concentration that causes a fail of reaction following a noxious stimuls in 50% of the patients. Similar results have been obtained when recording form neocortical pyramidal cells (see also: El-Beheiry et al., 1989, Exp. Brain Res, 75, 361-8).

Taken together, these findings suggest, that VAs reduce the excitability of cortical neurons by enhancing GABAergic inhibition. Since these effects occured (i) in a clinical range of concentration and (ii) followed the Meyer-Overton rule, a rule that correlates the potency of general anaesthetics in inducing general anaesthesia with their fat solubility, our findings may correlate with the loss of consciousness during anaesthesia. However, $GABA_A$ potentiating drugs like Benzodiazepines do not necessaryly induce GA, even when applied at high concentrations. Thus it remains to be illucidated, whether further mechanisms contribute in the case of VAs.