Etomidate alters the single-channel properties of $GABA_A$ receptors in newborn rat hippocampal neurons

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The $GABA_A$ receptor is a GABA activated chloride channel that belongs to the superfamily of cysteine-loop ligand-gated ion channels. The receptor is largely responsible for fast inhibitory neural transmission in the mammalian brain and is the target of many drugs including barbiturates, benzodiazepines and general anaesthetics such as etomidate. Etomidate is a carboxylated imidazole general anaesthetic. It is used as an induction agent in rapid sequence intubation in the emergency department because of its fast activation and hemodynamic stability (Bergen & Smith, 1997; Smith *et al.*, 2000).

Whole cell data has shown that etomidate modulates the $GABA_A$ receptor in a number of ways; at clinical concentrations (1-10μM) etomidate potentiates the $GABA_A$ receptor's response to GABA; at higher concentrations (10-1000μM) etomidate can directly activate and desensitize the receptor; and at even higher concentrations (>1000μM) it produces an inhibitory affect (Zhang *et al.*, 2002).

To investigate how etomidate affects the properties of single $GABA_A$ receptors single-channel currents activated by GABA and etomidate are being recorded from hippocampal pyramidal neurons. Neurons are cultured from newborn Wistar rats (<24hours old) and experiments performed from seven days after culture.

Preliminary results indicate that at clinical concentrations (1-10μM) etomidate potentiates the GABA induced current by increasing channel open time, open probability and channel conductance.

The ability of the general anaesthetic etomidate to increase the maximum channel conductance to >40pS adds to our growing list of drugs that are capable of affecting the conductance of $GABA_A$ receptors. Together with diazepam, pentobarbitone, propofol and now etomidate, which may all increase the maximum conductance of $GABA_A$ channels, our data suggest that such drugs are acting through a common molecular mechanism inherent in $GABA_A$ receptors.

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