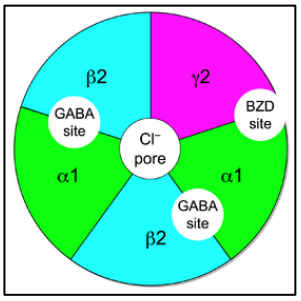
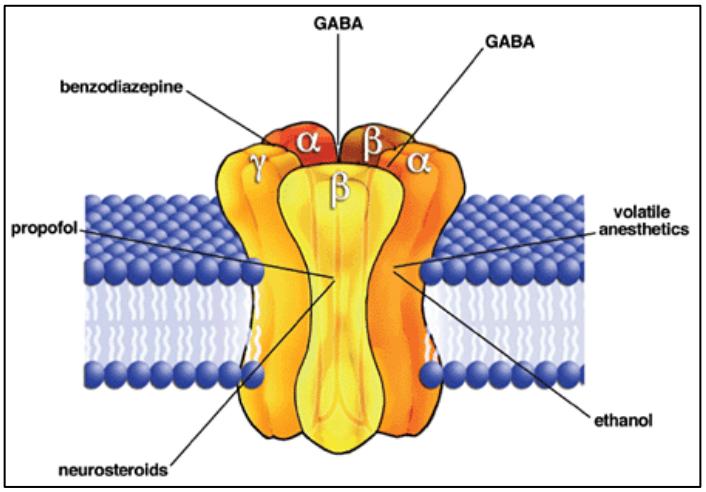
GABA Receptors: IV Anesthetics

Anesthetic Pearls: Anesthetic Implications of GABA Receptors and IV Anesthetics



I. **Overview**:

A major mechanism by which IV anesthetics: barbiturates, benzodiazepines, propofol, and etomidate (NOT opioids or ketamine) work is by an interaction at the GABA receptor. This interaction is by direct activation (increased binding) of **GABA** which is the major inhibitory neurotransmitter in the brain. This receptor controls a gate ion channel for chloride (Cl^-) that when activated allows the chloride ion to move inside the neuronal cell causing it to become hyperpolarized (more negative inside) and therefore resistant to neuronal excitation.



II. **GABA Receptor Structure**:

Model of the GABA – Benzodiazepine receptor channel complex. Current data suggest a pentameric protein composed of ***α***, ***β***, and ***γ*** subunits (the proposed arrangement of subunits is arbitrary). There are two sites for GABA binding at the **α / β-subunit interface** and a single site for benzodiazepine binding on the **α / γ-subunit interface**. Controversy exists on exact binding areas.

III. **How Does GABA Receptor Activation Result in the "Anesthetized State"?**

Fig. 1. The major pathways for sedative-hypnotics and analgesics in generating sedation and analgesia, respectively, which can combine to produce the anesthetic state. As indicated by the overlapping circles, the clinical effects of $GABA_A$ activation and neuronal Ca^{2+} channel inhibition are unlikely to be exclusive. Activation of the same cellular processes by the volatile anesthetics may explain much of their anesthetic action, although the common "unitary mechanism" remains to be described. In addition to activation of GABA Cl^- channels and inhibition of certain Ca^{2+} channels, the volatile anesthetics may decrease Ca^{2+} entry *via* excitatory glutamate receptors. Although the NMDA class seems particularly sensitive to ketamine, other glutamate-activated channels may be inhibited by the volatile agents. Volatile anesthetic effects also may be mediated in part by alteration of intracellular Ca^{2+} stores.