Does the organisation of native $GABA_A$ receptors affect their ion channel properties?

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The $GABA_A$ receptor is responsible for fast inhibitory neural transmission in the mammalian brain. Native Receptors are clustered at inhibitory synapses and are also found both clustered and non-clustered at other sites on the neuronal cell surface (extrasynaptic). The $GABA_A$ receptor is the target of many drugs including benzodiazepines such as diazepam and general anaesthetics such as etomidate. The functional behaviour of native $GABA_A$ receptors is complex. Much of the receptor's functional complexity has been attributed to its extensive structural heterogeneity (19 genes). The single channel properties of native $GABA_A$ receptors are different to recombinant $GABA_A$ receptors. The conductance of recombinant receptors never exceeds 40 pS and is not modulated by drugs unlike native receptors which have conductance's exceeding 80 pS and conductance may be modulated by drugs. However, when the trafficking protein GABARAP is coexpressed with recombinant $\alpha_1\beta_1\gamma_{2s}$ subsubunit receptors the channel properties mimic neuronal extrasynaptic $GABA_A$ receptors and their dispersion in the membrane changes such that they form clusters. We have used the patch clamp technique to compare the single channel properties of neuronal extrasynaptic $GABA_A$ receptors with recombinant $\alpha_1\beta_1\gamma_{2s}$ receptors ± GABARAP. We have found a linear correlation between higher conductances and longer mean open times in $GABA_A$ receptors from both native and recombinant systems. The results suggest that both receptor diversity and receptor organisation may play a role in the plasticity of the $GABA_A$ response.