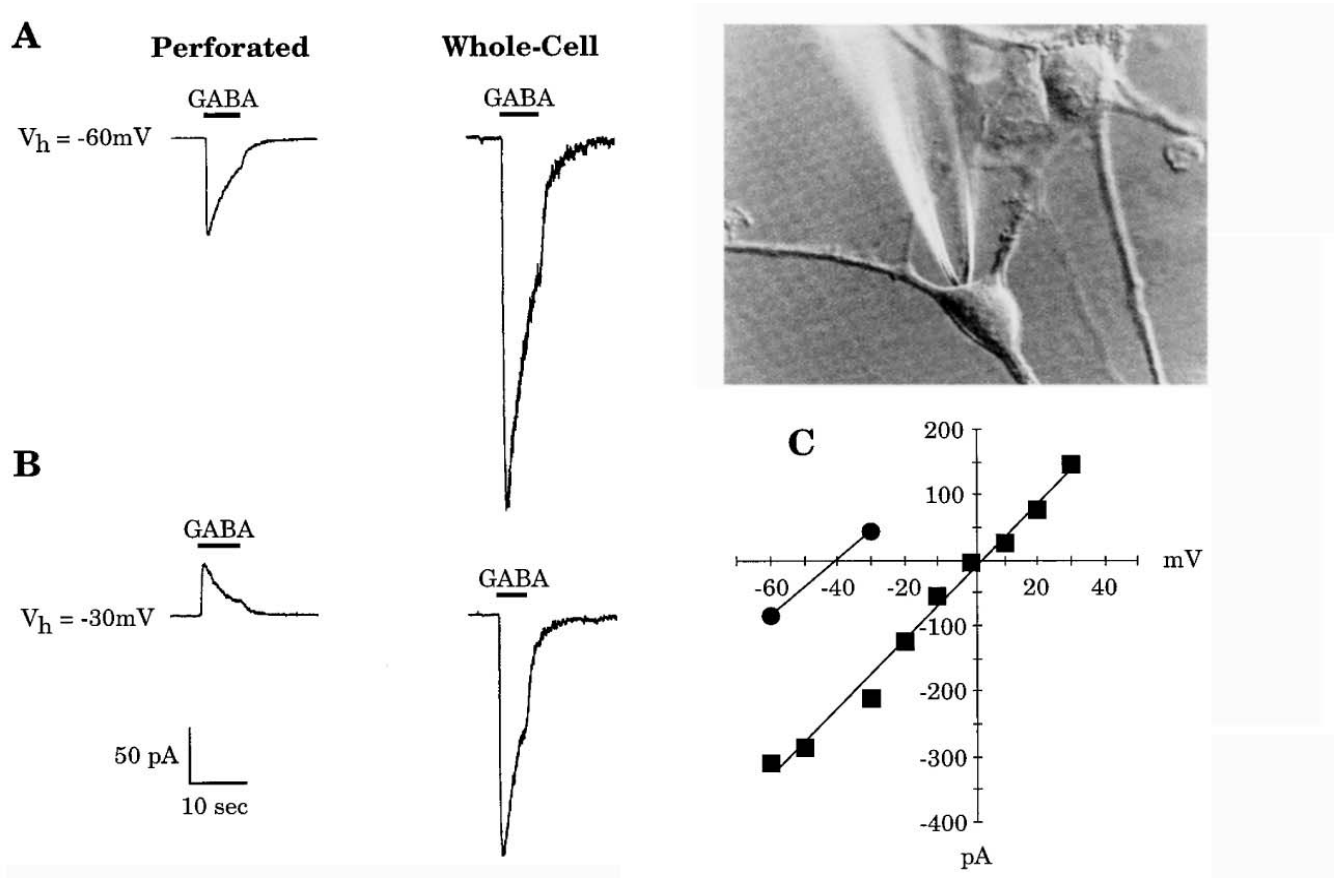
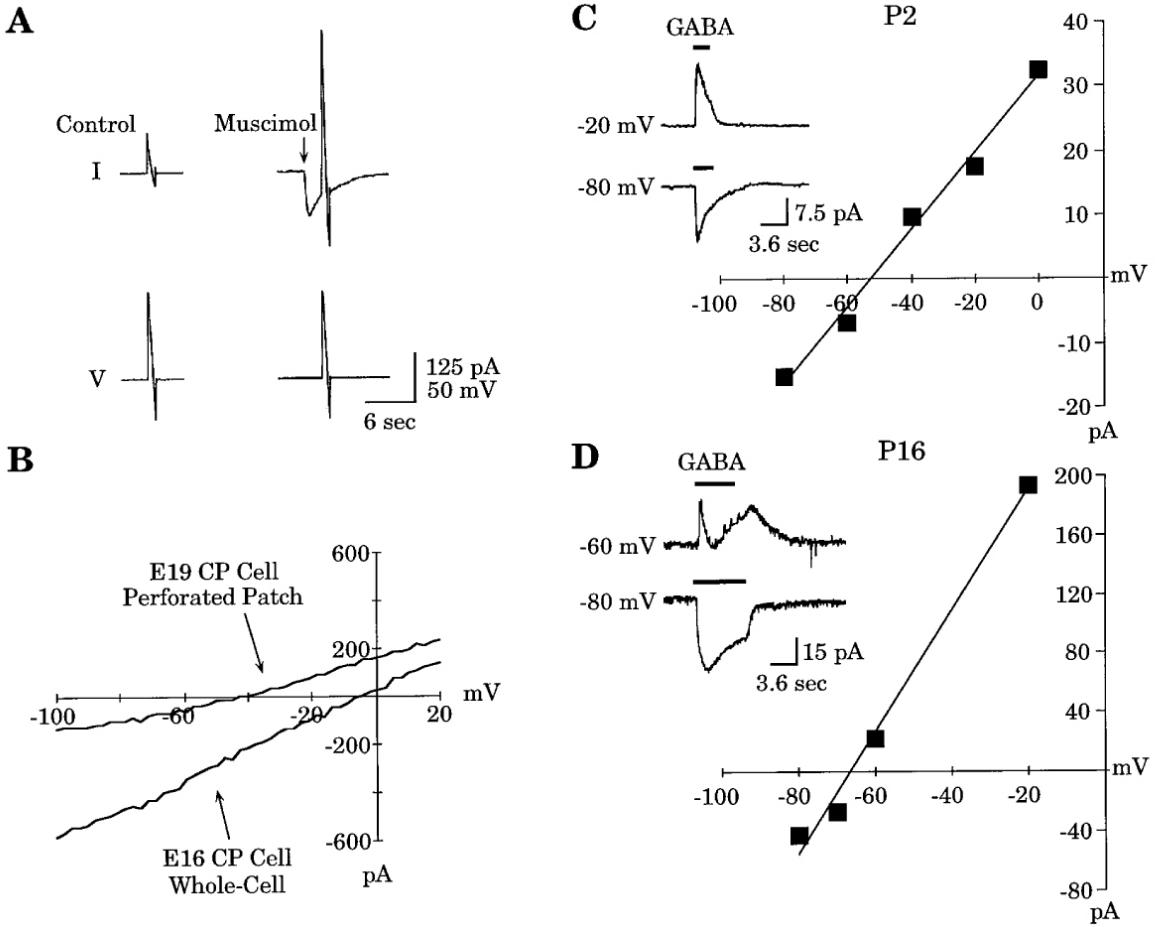
GABA reversal potential is different in

Perforated vs. Whole-cell patch recording methods

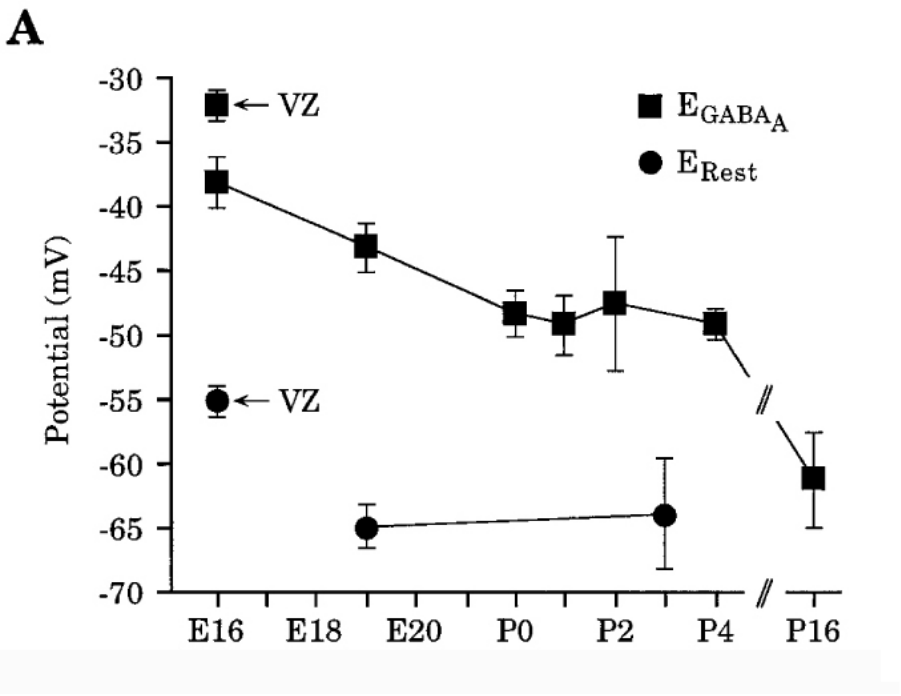


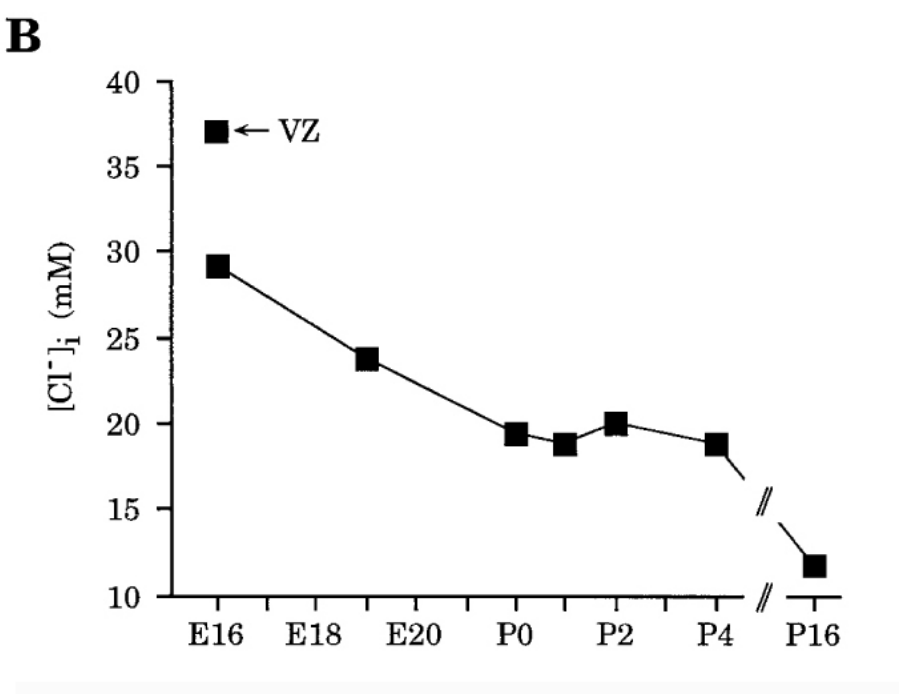
Gramicidin forms membrane pores that are exclusively permeable to monovalent cations and small, uncharged molecules, thus leaving internal Cl^- concentration undisturbed

$GABA_A$ Equilibrium Potential (E_{GABA_A}) is determined by two methods at various ages. Responses shift from monophasic to a more complicated trace due to maturation of $GABA_B$ receptor subtype

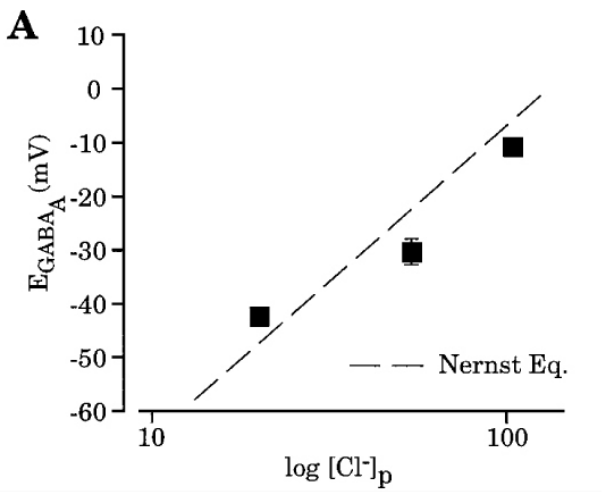


$GABA_A$ equilibrium potential declines over development, perhaps due to a fall in chloride ion concentration inside the cell.

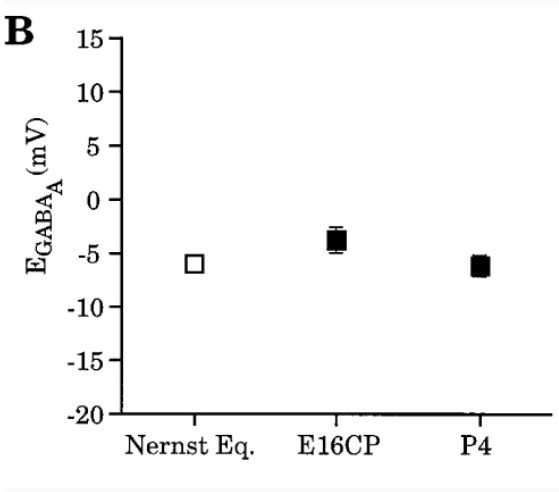




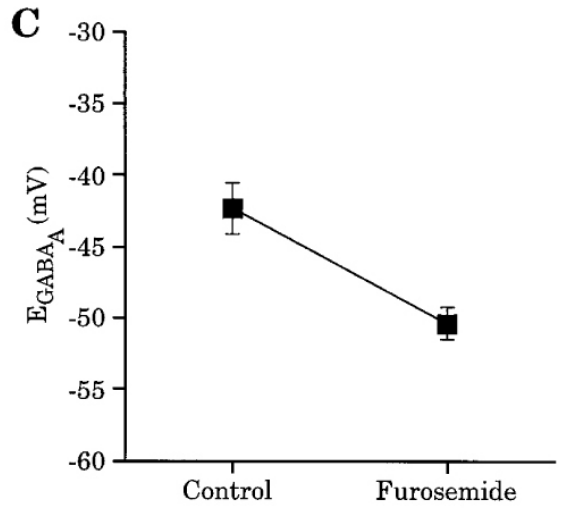
The chloride ion is the principle ion mediating $GABA_A$ receptor effects: the chloride gradient contributes significantly to E_{GABA_A}.



Whole-cell recordings used to bias the internal chloride conc. to that of the pipette, and muscimol (agonist) induced reversal potentials were measured. These values are compared to the reversal potential for chloride predicted by Nernst eq.

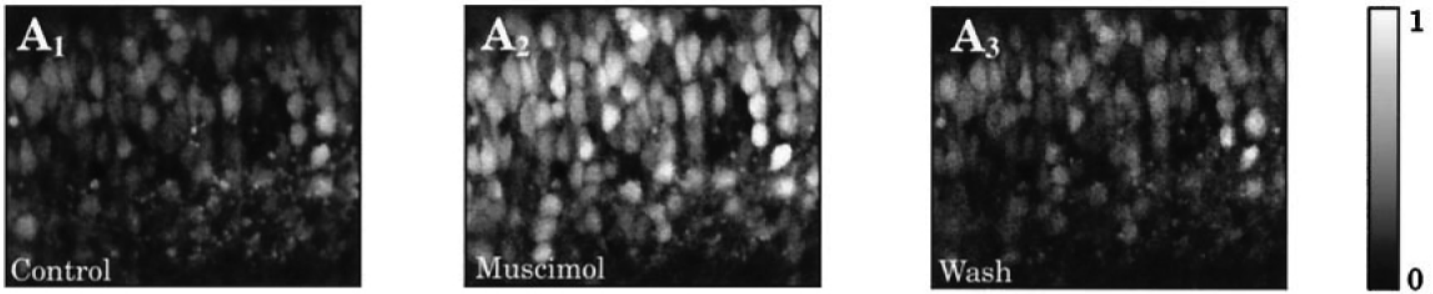


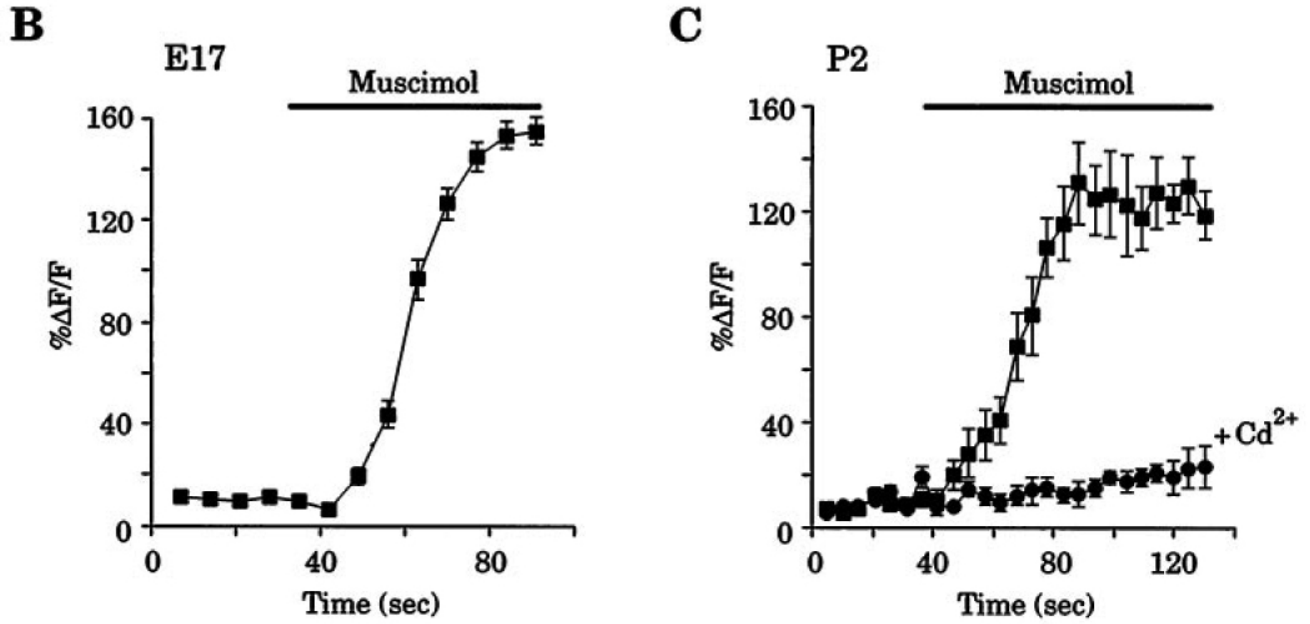
No developmental shift in E_{GABA_A} using whole-cell recording.



Perforated patch recordings Furosemide (chloride transporter blocker) reduces $GABA_A$ equilibrium potential.

More evidence for $GABA_A$ mediated membrane depolarization in early development : $GABA_A$ agonist causes reversible calcium entry through voltage-gated Ca^{++} channels.





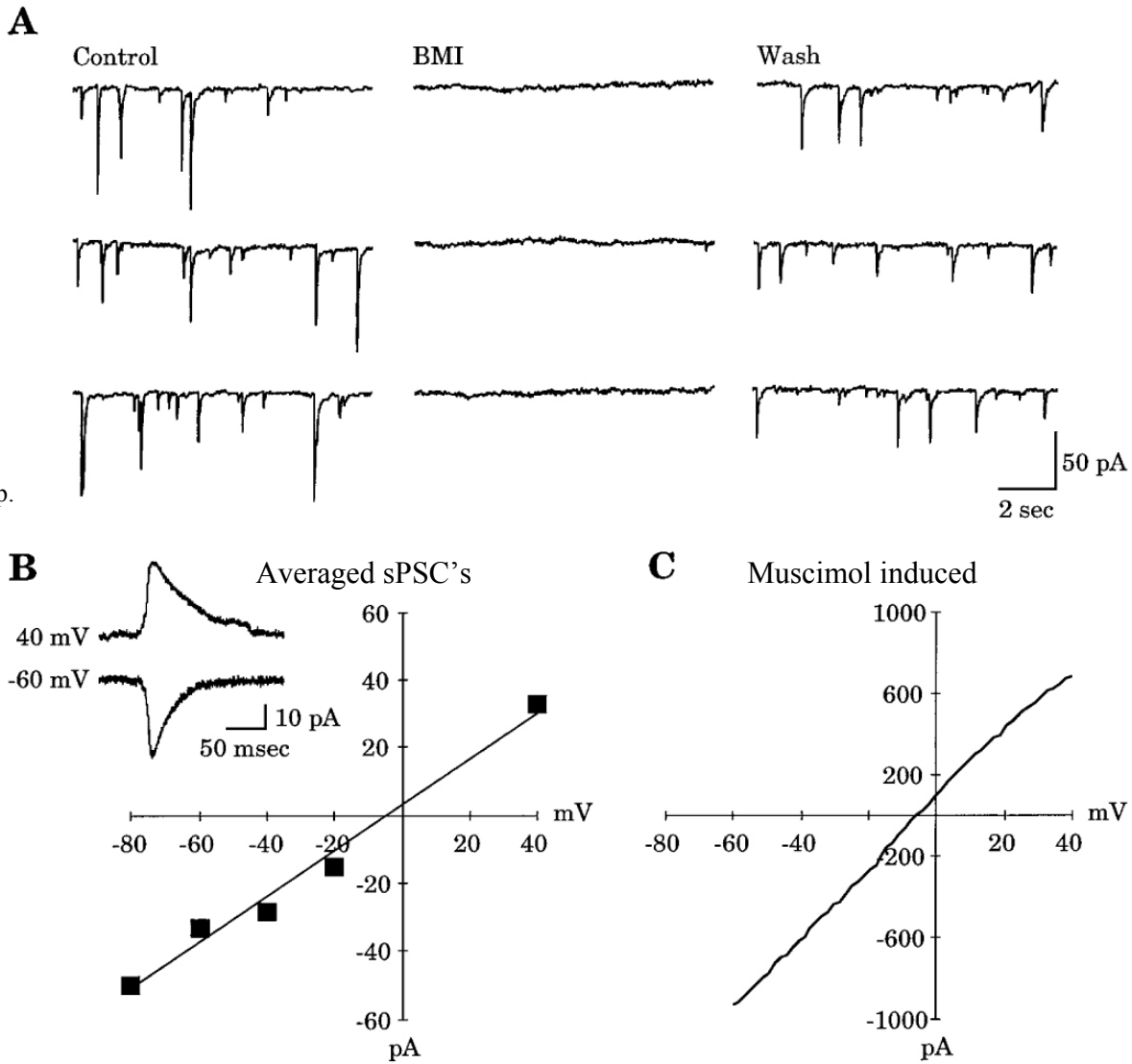
The reversal potential for endogenously active $GABA_A$-mediated synaptic current (sPSC) is nearly identical to the reversal potential for the exogenously applied $GABA_A$ agonist Muscimol.

These are not mini's:
TTX abolishes them

These sPSC's are not glutamatergic
CNQX and APV do not block.

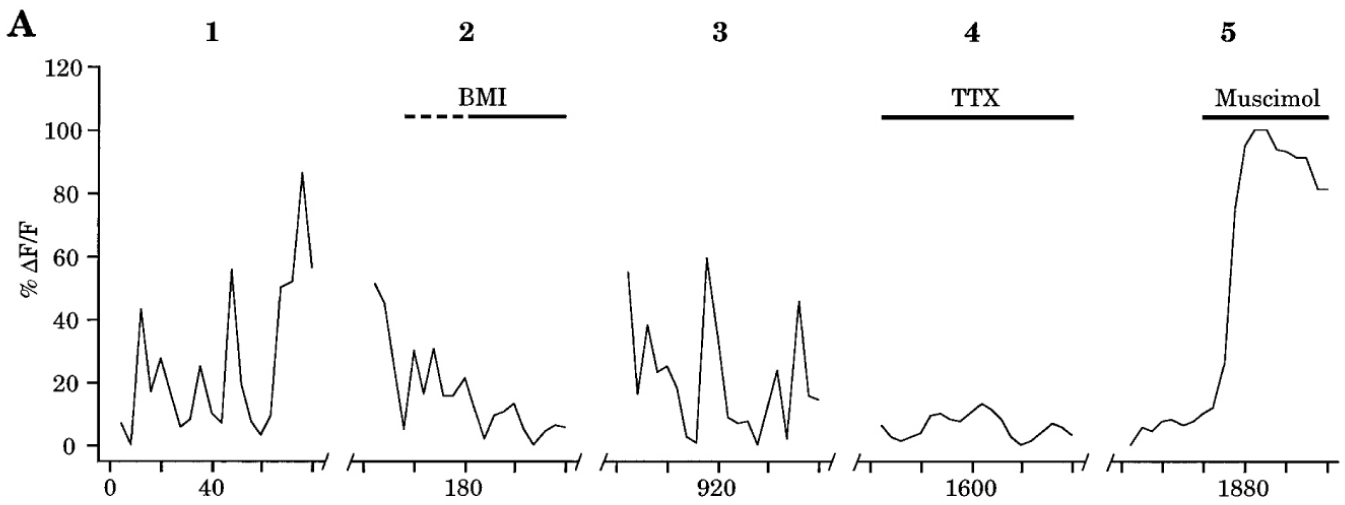
BMI= Bicuculline methiodide,
$GABA_A$ receptor antagonist.

A. whole-cell current clamp
B. Perforated patch voltage clamp.

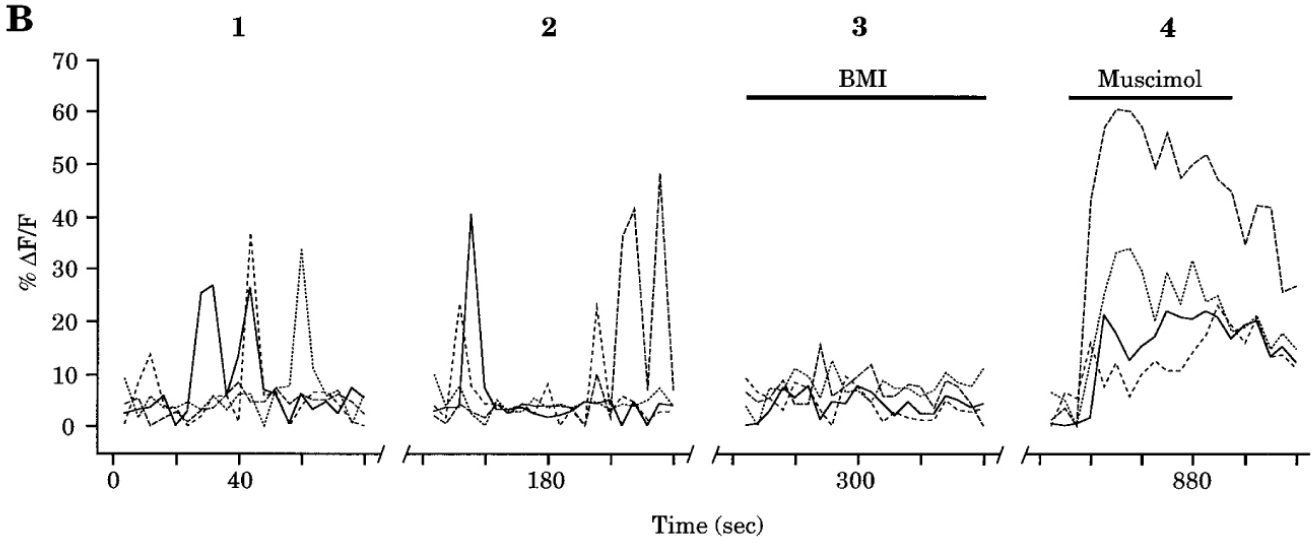


Spontaneous increases in intracellular calcium (measured by confocal calcium imaging) are mediated by $GABA_A$ receptor activation.

P1 neocortical (single cell)



P3 neocortical (combined data)



Conclusions:

Depending on the Cl^- equilibrium potential, the opening of $GABA_AR$ Cl^- channels may produce either a hyperpolarization or a depolarization.

Early in development, activation of $GABA_A$ receptors in CNS neurons produces membrane depolarization because of the elevated intracellular Cl^- concentration. This depolarization is sufficient to reach the threshold for action potential initiation and thus in immature neurons GABA may act as an excitatory neurotransmitter.

In sharp contrast, in adult neurons, $GABA_AR$ activation almost invariably causes either a membrane hyperpolarization or no potential change. In either case, the increase in membrane Cl^- conductance serves to clamp the membrane at E_{Cl} and so produces inhibition of neuronal activity.