On the idea the kinetics of $GABA_A$ receptor mediated synaptic currents control long range synchrony of 40 Hz oscillations in neocortex

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Developmental upregulation of the $GABA_A$ receptor α1 subunit causes a faster decay of GABAergic inhibitory postsynaptic currents (IPSCs) in the visual cortex around the time of eye opening. In α1 deficient mice, a juvenile type of $GABA_A$ receptors is retained during maturation. As a result the decay time of the IPSCs is longer in α1 -/- mice than in WT mice during the whole life span of the mice. Using voltage sensitive dye imaging, we monitored the spatiotemporal excitation patterning in visual cortex slices upon local stimulation of the network and found that in α1 -/- mice, the ability of the network to fire at 40 Hz is diminished compared to wild type mice. This observation was then substantiated in a simple integrate-and-fire model of the neocortex, where a selective shift in decay kinetics of the GABA synaptic currents adequately produced alterations in neuronal network activity similar to those observed in α1 -/-. Alterations in the wiring diagram of the neuronal network did not significantly affect this observation and also altering the ratio of pyramidal-to-interneurones used in simulations did not falsify the main hypothesis. Together these finding strongly support the idea that early onset of GABA synapse maturation is required for the normal neuronal network function in the maturating visual cortex. We are currently tested the effects of benzodiazepine agonists and inverse agonists on the experimentally induced spatiotemporal patterning of excitations in wild type mice.

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