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The role of GABAAR subunits in determining the time course of mIPSCs

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GABAergic neurotransmission is ubiquitous in the brain, controlling fundamental cellular processes such as shunting inhibition and network oscillations at different frequencies. The subunit composition of GABAA receptors (GABAAR) strongly affects the deactivation kinetics of GABA-evoked currents in recombinant systems, but it is less clear how it affects IPSC kinetics in situ. We addressed this issue by combining whole-cell recordings of miniature IPSCs with quantitative immunolocalization of synaptic GABAAR subunits. Neurons expressing only the $\alpha 1$ as synaptic α subunit have Zolpidem-sensitive mIPSCs with weighted decay time constants (τ_w) of 4-5 ms. Two other neuron types expressing only the $\alpha 2$ or the $\alpha 3$ as synaptic α subunit both exhibited slow, Zolpidem-insensitive mIPSCs with τ_w of 20 and 28 ms, respectively. In contrast, external tufted cells of the main olfactory bulb express two α subunit variants ($\alpha 1$ and $\alpha 3$) in their synapses. Quantitative analysis of confocal images revealed small within-cell, but large between-cell variability in synaptic $\alpha 1/\alpha 3$ subunit ratios. Whole-cell recordings demonstrated a small within-cell, but large between-cell variability in the decay of mIPSCs (τ_w varied from 3 to 30 ms) and the Zolpidem sensitivity correlated with τ_w . These results reveal that by mixing two subunits that confer very different τ_w , the kinetics of synaptic currents in individual cells can be tuned to any intermediate point within the whole range.