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Functions of extrasynaptic ionotropic glutamate and GABA receptors

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ABSTRACT OF THE TALK

High affinity extrasynaptic $GABA_A$ and NMDA receptors can detect ambient concentrations of endogenous agonists, GABA and glutamate, respectively. Extrasynaptic $GABA_A$ receptors have higher affinity to GABA and slower kinetics of desensitization and deactivation than synaptic receptors. Due to these properties they can mediate persistent 'tonic' current in neurons. This current changes input-output characteristics of individual neurons and has important effects on neuronal networks. We have found that in hippocampal interneurons tonic current is larger than in pyramidal cells due to less efficient GABA uptake in the vicinity of these cells. This suggests that tonic current can regulate synaptic inhibition in the hippocampus in cell type specific manner. While $GABA_A$ receptor mediated tonic current is present at physiological conditions, tonic current mediated by NMDA receptors could be obtained only when receptors are relived from voltage-dependent channel block by Mg^{2+}. Using two-photon calcium imaging we have demonstrated that extrasynaptic NMDA receptors in dendrites of hippocampal pyramidal neurons are pre-bound to ambient glutamate and mediate a proportion of calcium transients

during backpropagating action potentials. This happens because of transient relief of Mg^{2+} block at the time of action potential. Local glutamate uncaging paired with backpropagating action potential has further increased NMDA receptor dependent part of calcium transient. Such ‘extrasynaptic coincidence detection’ could be important for synchronisation of simultaneously firing neurons. In other words glutamate spillover from neighbouring synapses or glutamate release by astrocytes can be sensed specifically by neurons which fire at the same time.