Modulation of hippocampal inhibitory transmission by cannabinoids

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Marijuana affects brain function primarily by activating the G-protein-coupled receptor-1 (CB-1), which is expressed throughout the brain at high levels. Endogenous ligands of the CB1 receptor (endocannabinoids) have been identified and shown to modulate glutamatergic and GABAergic transmission via the CB1 receptor.
In the hippocampus the CB1 receptors are mainly present presynaptically on the GABAergic interneurons where they depress inhibitory transmission. Pilot experiments suggest that there might be also a postsynaptic effect. Do cannabinoids act directly on synaptic receptors other then CB1?
In this study, synthetic cannabinoid WIN 55212-2 has been found to accelerate decay kinetics of the glycine- and GABA-induced postsynaptic current in the isolated hippocampal pyramidal cells using cell patch clamp approach. Currently we are working at examining possible direct effects of cannabinoid ligands on the GABA and glycine receptors in inhibitory synaptic transmission in the hippocampal slices using paired recordings of interneurons and pyramidal cells of the hippocampal CA1 region. We hypothesise that accelerating of the decay of the GABAergic current may contribute to overall depressing effect that cannabinoids have on inhibitory transmission. The general effect would be that of desinhibition of the pyramidal CA1 neurons that constitute the output of the hippocampus.

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Poster Neuroscience 2