

Tatiana Golovko
Dr. med.

Suppression of inhibition by a direct action of cannabinoids on ionotropic GABA_A receptors

Geboren am 28.06.1973, in Irkutsk, Russland
Diplom der Ärztin im Fach Humanmedizin am 27.02.1998 an der Staatliche medizinische Universität Irkutsk, Fakultät für Humanmedizin, Russland

Promotionsfach: Physiologie und Pathophysiologie

Doktorvater: Prof. Dr. Andreas Draguhn

Cannabinoids have been shown to regulate inhibitory synaptic transmission via activation of presynaptic G-protein-coupled cannabinoid CB₁ receptors (CB₁Rs). Here we report that cannabinoids can also suppress inhibition by a direct action on postsynaptic ionotropic GABA_A receptors (GABA_ARs). Cannabinoids reduce amplitude and modulate kinetics of currents mediated by both recombinant and native GABA_ARs in isolated cells. Paired recordings from rat neocortical slices confirm these observations in GABAergic synapses between fast spiking interneurons and pyramidal neurons. In the presence of a CB₁R antagonist endocannabinoids released from pyramidal neurons by a train of depolarising pulses transiently inhibit evoked IPSCs with a recovery time several-fold faster than that for conventional CB₁R-dependent depolarization induced suppression of inhibition. Suppression of GABA_ARs by cannabinoids reduces the influence of GABAergic interneurons on the firing of pyramidal neurons. Thus CB₁R-independent modulation of GABA_ARs by cannabinoids provides a novel mechanism for tonic and activity-dependent regulation of synaptic inhibition.