Prospects for the use of cannabinoids in the treatment of epilepsy

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There is broad evidence on the protective activity of synthetic cannabinoid agonists against a variety of chemoconvulsants or electroconvulsions in rodents. The interactions between cannabinoid agonists (WIN 55,212-2 mesylate – non-selective CB_1 and CB_2 receptor agonist or ACEA – a selective CB_1 receptor agonist) and antiepileptic drugs (AEDs) have been evaluated. In the mouse maximal electroshock model, ACEA (in subthreshold doses and always co-administered with a fatty-acid amide hydrolase inhibitor) potentiated the anticonvulsant action of conventional AEDs, valproate and phenobarbital and a newer AED, pregabalin. In no case, the adverse effects of AEDs (impairment of motor coordination, long-term memory and muscular strength) were enhanced by ACEA. As regards WIN 55,212-2 mesylate, it potentiated the anticonvulsant activity of carbamazepine, phenobarbital, phenytoin, valproate (classical AEDs) and that of lamotrigine, pregabalin and topiramate (newer AEDs). In all cases of the combinations with classical AEDs, profound neurotoxic effects were evident. Combinations with newer AEDs were free from pharmacokinetic mechanisms or neurotoxic effects. The initial clinical data on the add-on treatment with cannabidiol (a non-psychoactive cannabinoid) indicate that in 23 children and young adults with drug-resistant epilepsy, there was a 39% reduction in responder rate and 17% of patients were seizure free. The most frequent adverse effects included somnolence (57%), fatigue (57%) and increased concentrations of concomitant AEDs (22%). The experimental data point to the beneficial interactions of cannabinoid agonists with newer AEDs. More clinical data are required before reliable conclusions can be drawn on this issue. Supported by DS 475.