RESEARCH PAPER

Cannabinoids inhibit cholinergic contraction in human airways through prejunctional CB_1 receptors

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Background and Purpose

Marijuana smoking is widespread in many countries, and the use of smoked synthetic cannabinoids is increasing. Smoking a marijuana joint leads to bronchodilation in both healthy subjects and asthmatics. The effects of Δ^9-tetrahydrocannabinol and synthetic cannabinoids on human bronchus reactivity have not previously been investigated. Here, we sought to assess the effects of natural and synthetic cannabinoids on cholinergic bronchial contraction.

Experimental Approach

Human bronchi isolated from 88 patients were suspended in an organ bath and contracted by electrical field stimulation (EFS) in the presence of the phytocannabinoid Δ^9-tetrahydrocannabinol, the endogenous 2-arachidonoylglycerol, the synthetic dual CB_1 and CB_2 receptor agonists WIN55,212-2 and CP55,940, the synthetic, CB_2-receptor-selective agonist JWH-133 or the selective GPR55 agonist O-1602. The receptors involved in the response were characterized by using selective CB_1 and CB_2 receptor antagonists (SR141716 and SR144528 respectively).

Key Results

Δ^9-tetrahydrocannabinol, WIN55,212-2 and CP55,940 induced concentration-dependent inhibition of cholinergic contractions, with maximum inhibitions of 39, 76 and 77% respectively. JWH-133 only had an effect at high concentrations. 2-Arachidonoylglycerol and O-1602 were devoid of any effect. Only CB_1 receptors were involved in the response because the effects of cannabinoids were antagonized by SR141716, but not by SR144528. The cannabinoids did not alter basal tone or contractions induced by exogenous Ach.

Conclusions and Implications

Activation of prejunctional CB_1 receptors mediates the inhibition of EFS-evoked cholinergic contraction in human bronchus. This mechanism may explain the acute bronchodilation produced by marijuana smoking.

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