THE CANNABINOID ANTAGONIST SR 141716A REDUCES THE INCREASE OF EXTRA-CELLULAR DOPAMINE RELEASE IN THE RAT NUCLEUS ACCUMBENS INDUCED BY A NOVEL HIGH PALATABLE FOOD

Melis Tiziana, Sanna Fabrizio, Succu Salvatora, Argiolas Antonio, Melis Maria Rosaria

Beranrd B. Brodie Department of Neurosciences, University of Cagliari, Italy

SR 141716A is the first selective cannabinoid CB1 receptor antagonist become available for researchers in the cannabinoid field. This compound and many others more or less releted have been synthesized and are studied for understanding the role of endocannabinoids and their receptors in numerous physiological functions and are tested in clinical trials for a possible use in diseases such as obesity, nicotine and alcohol addictions. SR 141716A has been reported to reduce food intake either in humans or in laboratory animals. Since food exerts its pleasurable and reinforcing effects by increasing the activity of mesolimbic dopaminergic neurons which project from the ventral tegmental area to the nucleus accumbens, the inhibitory effect of SR 141716A on food intake may be related to its ability to reduce the increase of dopaminergic mesolimbic neurons induced by novel and high palatable food. In order to verify such hypothesis, we studied the effect of SR 141716A on dopamine content in the dialysate of the nucleus accumbens shell of rats put in the presence of a novel and high palatable food (a candied cherry).
As expected, the introduction into the experimental cage of a novel high palatable food, but not of a normal chow pellet, induced rats to approach, lick and eat it, and these behavioral responses were concomitantly with an increase in dopamine and DOPAC concentrations in the dialysate of the nucleus accumbens shell. SR 141716A given 15 min before exposition to the candied cherry at the doses of 0.3 mg/kg i.p. and 1 mg/kg i.p., which per sé did not modify dopamine levels, reduced the increase in dopamine and DOPAC concentration in the nucleus accumbens shell dialysate. This inihibitory effect of SR141716A was prevented by WIN55,512-2 (0.3 mg/Kg i.p.) and HU-210 (0.1 mg/Kg i.p.), two potent cannabinoid CB1 receptor agonist, given 15 min before SR 141716A, at doses that are unable per se to modify dopamine concentration in the nucleus accumbens shell. In conclusion, the present results show for the first time that SR 141716A reduces the activation of mesolimbic dopamine system induced by a novel high palatable food and suggest that cannabinoid CB1 receptor antagonists exert their inhibitory effect on feeding and ingestive behaviour by reducing the pleasurable and rewarding effects of food.