

## **Modulation of nicotinic acetylcholine receptors by cannabinoids.**

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The recent legalization of medicinal and in some cases recreational use of marijuana by many states in the USA, has resulted in a significant increase in the use of both marijuana and tobacco. Studies have implicated the use of marijuana with the addictive potential of tobacco and viceversa suggesting that the mechanism of action of the addictive substances in both, cannabinoids and nicotine, interact with each other in the brain. However, little is known about the effects that the phytocannabinoids found on marijuana have on the function of nicotinic acetylcholine receptors (nAChRs). Interestingly, it has been shown that endogenous cannabinoids are able to modulate the function of the two most abundant nAChRs in the brain the  $\alpha 7$  nAChR and the  $\alpha 4\beta 2$  nAChR. The two most abundant phytocannabinoids in marijuana  $\Delta^9$ -Tetrahydrocannabinol (THC) and cannabidiol (CBD) have been shown to have tremendous therapeutic potential in many neurological disorders such as convulsions and pain. However, many of their therapeutic effects are not associated with the activation of the cannabinoid system. Which is why there is a critical need to increase our understanding of the molecular targets of phytocannabinoids in order to increase our chances of using them successfully in the clinic. Interestingly, one report describes cannabidiol (CBD) as a negative allosteric modulator of the  $\alpha 7$ nAChR. Here we are proposing to use primary hippocampal neuron cultures as a model system to study the effects of THC and CBD, and their combinations, have on the function of nAChRs of different subunit compositions.